

Poster Presentations Oesophageal, gastric and duodenal disorders

Oesophageal, gastric and duodenal disorders

09:00-19:00 / Poster Exhibition

P0001

SERUM ADIPOKINES AS NON-INVASIVE BIOMARKERS IN CROHN'S DISEASE

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Introduction: Adipose tissue wrapping the gastrointestinal tract is a risk factor for disease activity in Crohn's disease (CD). Indeed, adipokines associated to lipid metabolism can modulate local immune responses. However, few studies have investigated the possible association between adipokines and CD.

Aims & Methods: Here, we aimed to evaluate the role of serum adipokines as possible biomarkers in CD.

Serum samples were obtained from 18 patients with endoscopically active CD (aCD), 22 patients with endoscopically quiescent CD (qCD) and 36 non-inflamed healthy controls (HC). All serum samples were obtained from CD patients and HC at the moment of colonoscopy in Hospital Universitario La Princesa, Madrid, Spain. The Simple Endoscopic Score for Crohn's Disease (SES-CD) was determined during colonoscopy in all CD patients in order to classify them as aCD (SES-CD ≥ 3) or qCD (SES-CD ≤ 2). Demographic variables (i.e. sex, age and BMI) were analysed by chi square test (frequencies) or ANOVA test (means). Serum leptin, ghrelin, resistin and adiponectin were analysed by Multiplex (Bio-Rad, Hercules, CA, USA) in a Luminex 200 system technology following manufacturer's instructions. The final concentration value of each adipokine was the result of the mean from the two duplicated measures. Adipokines normality was tested and adipokines were natural log transformed. Spearman correlation was performed for the adipokines. Adipokine means for each group of patients were compared by ANOVA test. Median and interquartile range for each patient group was determined for those skewed adipokines and Kruskal-Wallis test was performed. Receiver Operating Characteristic (ROC) curves and the area under the curve (AUC) were carried on to evaluate the discriminatory capacity of the adipokines levels between study groups. The Youden cut-off index got from the ROC curve was matched with the adipokines concentration. Furthermore, for those adipokines that showed an AUC > 0.7 , a binary logistic regression adjusted by possible confounders (i.e sex, age, BMI) was performed in order to test their possible association with CD.

Results: No differences were found in age, sex or BMI among aCD, qCD and HC. There was no correlation among the adipokines analyzed. Means distribution for serum resistin was different among aCD, qCD and HC

($p=0.02$). However, only comparisons between aCD and HC a groups showed significant differences ($p=0.03$) in the post hoc test. Serum leptin, ghrelin and adiponectin did not show differences between means. ROC curve for resistin showed an AUC along with its 95% confidence interval of 0.75 (0.61-0.89) when HC and aCD groups were compared. Furthermore, in this case, as sensitivity and specificity for Youden index correspond to the total resistin median concentration (9822pg/ml), this value was selected as a cut-off for the binary logistic regression analysis; thus, odds ratio (OR) along with their 95% confidence interval analysis of high relative resistin levels (values higher than total resistin median) adjusted by age, sex and BMI yielded a value of 5.46 (1.34-22.14) when active patients were compared to HC. Comparisons between qCD and aCD or between qCD and HC showed an AUC < 0.7 . ROC curves analysis for leptin, ghrelin and adiponectin did not show enough accuracy to discriminate between groups.

Conclusion: Resistin may modulate the inflammation state in CD and it is probably associated to activity, being this association independent of sex, age or BMI. Resistin may work as a serum biomarker of activity in CD.

Disclosure: Nothing to disclose

P0002 WITHDRAWN

P0003

REDEFINING PATTERNS OF TUMOUR RESPONSE TO CHEMORADIO THERAPY IN OESOPHAGEAL CANCER WITH THE AID OF AI

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Introduction: Tumour response has been categorized in many ways with in-and-between tumour types. In order for tailored treatment decisions to be made, there is a need for a reproducible, objective and standardized assessment of response which combines histological patterns and downstaging.

Aims & Methods: Our cohort was composed of 100 patients with oesophageal adenocarcinoma (cT2-T3) treated with chemoradiotherapy. Three H&E slides per patient were analysed by a panel of pathologists and run through an algorithm to determine tumour cell percentage (TC%), size and distance between tumour fragments. Clinical data was used to determine correlations to survival and recurrence.

Results: Four histological patterns of regression were distinguished; fragmented (clustered or scattered), shrinkage and no-response. TC% was found to be significantly higher in clustered fragmentation subtype compared to scattered subtype in the mucosa ($p=0.04$) and tended to be higher in submucosa ($p=0.08$), muscularis ($p=0.15$) and subserosa ($p=0.32$). Preliminary results were obtained with only 70 patients, which we hope to increase to 100.

Conclusion: By using trained algorithms it is possible to accurately determine subtypes of patterns of response in an unbiased approach which might form the basis of predictive biomarker research. Recognition of these patterns of response and correlation with clinical outcome could provide a useful prognostic marker for further treatment. Moreover, our algorithms might be transferable to other cancer types.

Disclosure: Nothing to disclose

P0004

SIGNIFICANCE OF ESTROGEN RECEPTOR EXPRESSION IN ESOPHAGEAL ADENOCARCINOMA: PROOF OF CONCEPT

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Introduction: Estrogens play a crucial role in the development and progression of multiple types of cancer. Estrogen signaling through nuclear estrogen receptors (ERs), i.e. ERα and ERβ as well as membrane-bound estrogen receptor, i.e. G protein-coupled estrogen receptor (GPER), participates in the regulation of cancer cell proliferation and migration. However, the importance of estrogen receptors in esophageal adenocarcinoma is elusive.

Aims & Methods: To better assess the significance of estrogen receptors in esophageal adenocarcinoma, bioinformatic analysis was performed using datasets provided by Global Expression Omnibus and The Cancer Genome Atlas Esophageal Carcinoma from The Cancer Genome Atlas. Gene expression correlation was carried out with the Genevestigator co-expression tool. Pathway enrichment was evaluated with The Kyoto Encyclopedia of Genes and Genomes pathway using functional annotation of The Database for Annotation, Visualization and Integrated Discovery. Survival analysis was determined with Kaplan-Meier plotter.

Results: Gene expression profiling of estrogen receptors using dataset from Global Expression Omnibus revealed deregulation of ERα, ERβ and GPER expression in esophageal adenocarcinoma. Pathway enrichment analysis confirmed that estrogen receptors are correlated with genes participated in metabolic pathways, *S. aureus* infection, complement and coagulation cascades, oxidative phosphorylation, neurodegenerative diseases, spliceosome and ribosome biology as well as RNA transport. The Kaplan-Meier analysis documented poor overall survival in esophageal carcinoma patients with lower expression of ERα. In contrast, lower expression of GPER seems to be associated with better overall survival in esophageal adenocarcinoma patients.

Conclusion: In the present study, we found alterations of estrogen receptors expression and a relationship between the level of estrogen receptors and genes involved in numerous essential processes in the neoplastic transformation of esophagus. Moreover, our analysis highlighted prognostic significance of ERα and GPER expression in esophageal adenocarcinoma patients. These findings point to the need of a better understanding on the role exerted by estrogen receptors in esophageal adenocarcinoma.

Disclosure: Nothing to disclose

P0005

MITOCHONDRIA-TARGETING HYDROGEN SULFIDE-RELEASING AP-39 IN PREVENTION OF CHEMICALLY-INDUCED GASTRIC MUCOSAL DAMAGE

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Introduction: Hydrogen sulfide (H₂S) is an endogenous gaseous mediator produced by L-cysteine metabolism due to the activity of particular enzymatic pathways. This molecule has been shown to affect mitochondrial complexes and in result to modulate anti-oxidative mechanisms. Interestingly, H₂S-releasing pharmacological tools were shown to play a key role within digestive system pathophysiology exerting anti-inflammatory and anti-oxidative activity. Taking into account the experimental data, beneficial effects of H₂S is strictly dose-dependent and the controlled release of this molecule seems to be crucial to avoid cytotoxicity and to obtain desired biological effects. Thus, we aimed to assess the effect of mitochondria-targeting H₂S-releasing compound, AP-39 administered i.g. against the development of aspirin- or ethanol-induced GI damage.

Aims & Methods: Wistar rats were pretreated with vehicle, AP-39 (0.004-2.5 mg/kg i.g.) or NC-AP-39 as structural control to AP-39 without ability to release H₂S. After 30 min, gastropathy was induced by aspirin (125 mg/kg i.g.) or 75%-ethanol (1.0 ml, i.g.). Gastric lesions area and gastric blood flow (GBF) were determined by planimetry, histology and laser flowmetry, respectively. Gastric mucosal mRNA expressions of COX-1, COX-2, iNOS, annexin-A1 and TGF-β1 as well as serum contents of TGF-β1, TGF-β2, and TGF-β3 were determined by real-time PCR or Luminex platform, respectively. Gastric mucosal PGE₂ content was determined by ELISA.

Results: Pretreatment with AP-39 (0.02 mg/kg i.g.) reduced gastric damage area induced by both, aspirin or ethanol with accompanied increased in GBF level. AP-39 decreased upregulated gastric mucosal mRNA expression for pro-inflammatory iNOS and maintained upregulated mRNA expression for anti-inflammatory annexin-A1 in gastric mucosa exposed to aspirin or ethanol. AP-39 decreased serum concentration of TGF-β1 and TGF-β2 but did not affect PGE₂ content in gastric mucosa administered with aspirin or ethanol. NC-AP-39 did not prevent gastric mucosa in tested experimental models.

Conclusion: We conclude that mitochondria-targeting and H₂S-releasing AP-39 applied i.g. exerts gastroprotective effect dose-dependently affecting gastric microcirculation. This compound seems to be promising for the further studies related to the role of hydrogen sulfide in regulation of mitochondrial complexes activity in pathophysiology of GI tract.

Disclosure: Nothing to disclose

P0006

TRACKING THE SOMATIC GASTRIC CANCER TISSUE MUTATIONS IN THE BLOOD: PROPORTION OF THE PATIENTS WITH DETECTABLE ALTERATIONS AND ASSOCIATION WITH ONCOPROTEINS

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Introduction: Gastric cancer (GC) is one of the most common and lethal oncological diseases of the gastrointestinal tract worldwide (Ferlay et al. 2015). Determination of specific and individual molecular multi-layer “signatures” has been shown to be pivotal for prediction, diagnosis and monitoring of various cancers, with implications for precision medicine (Cohen et al. 2018). Since the discovery of the circulating plasma cell-free DNA (cfDNA) the origin and characteristics of cfDNA were extensively studied. It was shown that cfDNA could harbour genetic aberrations from malignant tissue. However, there is a lack of comprehensive studies conducted in GC. **Aims & Methods:** GC tissue and blood were collected from 30 patients who were recruited at the Department of Gastroenterology, Lithuanian University of Health Sciences Hospital. Tumour tissue samples were obtained from the primary lesion of the resected specimen or biopsy and stored at -80 °C as a fresh-frozen sample. Peripheral blood was drawn at admission (before surgery), centrifuged and stored at -80 °C until DNA isolation. Genomic DNA from primary lesion was isolated using Qiagen miRNeasy Mini kit and DNA from white blood cells (WBC) was isolated using salting-out method. Total circulating nucleic acids from plasma were extracted using column based QIAamp Circulating Nucleic Acid isolation kit according to the manufacturers’ protocol. Whole exome sequencing (WES) was performed for GC patients’ tissue and paired WBC samples using IDT xGen Exome Research Panel and pair-end sequenced (2 x 100 bp) on NovaSeq 6000 platform. Targeted NGS using IDT xGen Custom Panel consisting of 38 gastric cancer-associated genes selected according WES results was performed for GC plasma cfDNA only. cfDNA libraries were pair-end sequenced (2 x 150 bp) on NovaSeq 6000 platform. Serum level of oncoproteins (CEA, CA19-9 and CA72-4) was measured with enzyme-linked immunosorbent assay (ELISA) in patients’ serum upon admission to the hospital.

Results: After WES was performed for GC tissue and normal WBC samples, in total for 23 of 30 patients (76.7 %) mutations associated with GC were determined. The most frequently mutated genes in our study were *TP53*, *FAT4*, *GLI3*, *APC*, *KMT2C*, *SYNE1*, *EPHB1*, *PIK3CA*, and *TRRAP*. Matching tissue and cfDNA alterations were detected for 14 of 23 (60.9 %) GC patients. A total of 121 variants in cell-free DNA, 202 variants in tumour samples and 40 matching alterations were detected. Tissue matching alterations in plasma were detected in genes: *TP53*, *ERBB2*, *FAT1*, *MLH1*, *FAT4*, *SPEN*, *KMT2C*, *MUC16*, *ACVR2A*, *ERBB4*, *PREX2*, and *SYNE1*. Matching tumour and plasma alterations were detected significantly more often in samples of the patients with larger tumours (55.6 % and 10.0%, T3-T4 and T1-T2 respectively, $p=0.018$). Number of detected alterations moderately correlated with age ($R=0.38$, $p=0.048$; $R=0.47$, $p=0.012$; and $R=0.40$, $p=0.035$; respectively number of matching alterations; tissue and plasma alterations). Specific mutations and levels of oncoproteins were analysed for discriminating T and M status. Levels of CEA correlated with total cfDNA yield ($R=0.38$, $p=0.041$) and was observed in higher levels for poorly differentiated adenocarcinoma cases ($p=0.045$).

Conclusion: Our results show, that tissue and cfDNA matching mutations were mostly detected for GC patients with larger tumours and in combination with different molecular analytes may enable cfDNA analysis for monitoring of the GC patients’ disease state.

References: 1. Ferlay, Jacques et al. 2015. “Cancer Incidence and Mortality Worldwide: Sources, Methods and Major Patterns in GLOBOCAN 2012.” *International Journal of Cancer* 136(5): E359-86. 2. Cohen, Joshua D. et al. 2018. “Detection and Localization of Surgically Resectable Cancers with a Multi-Analyte Blood Test.” *Science* 359(6378): 926-30.

Disclosure: Nothing to disclose

P0007

LEUKAEMIA INHIBITORY FACTOR SIGNALLING FOR TARGETING CANCER STEM CELLS IN GASTRIC ADENOCARCINOMA

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Introduction: Cancer stem cells (CSCs) present intrinsic chemo-resistance mechanisms contributing to tumour maintenance and recurrence, making their targeting of utmost importance in cancer therapy. The Hippo pathway has recently been implicated in gastric CSC properties. And some studies have shown that it can be regulated by Leukaemia Inhibitory Factor Receptor (LIFR) and its ligand LIF. Interestingly, the impact of LIF on gastric CSCs has never been investigated. Consequently, this study aimed to determine the effect of LIF on CSC phenotype and properties in GC cell lines and patient derived xenograft (PDX) cells.

Aims & Methods: RTqPCR, 3D tumoursphere assays as well as immunofluorescence analysis were used to decipher the effect of LIF treatment on gastric CSC markers expression, tumoursphere formation and regulation of the Hippo pathway and LIF/LIFR canonical JAK/STAT pathway were evaluated.

Results: Results indicate that LIF treatment decreased gastric tumorigenic and chemo-resistant CSC population, in both GC cell lines and PDX cells. In addition, LIF increased activation of LATS1/2 Hippo kinases thereby decreasing downstream YAP/TAZ nuclear accumulation, TEAD transcriptional activity and target gene expression. LIF anti-CSC effect was reversed by Hippo kinase inhibition but not by JAK/STAT inhibition, highlighting the opposite effects of these two pathways downstream LIFR.

Conclusion: In conclusion, this study shows for the first time that LIF displays anti-CSC properties in GC and relates this effect to the activation of Hippo kinases LATS1/2. LIF treatment could *in fine* constitute a new CSCs-targeting strategy to help decrease relapse cases and bad prognosis in GC.

Disclosure: Nothing to disclose

P0008

CAN NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) BE A SIMPLE PREDICTIVE MARKER FOR GASTRIC INTESTINAL METAPLASIA?

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Introduction: Gastric intestinal metaplasia (GIM) and gastric atrophy (GA) are pre-neoplastic lesions that can lead to gastric cancer (GC). The diagnosis of GIM and GA usually based on endoscopic and histopathological findings (1). Nowadays, there are no recognized good biomarkers of GIM and GA. The neutrophil-to-lymphocyte ratio (NLR) is an economical, effective, and repetitive indicator of inflammation (2). In this study, we aimed to comparatively evaluate red cell distribution width (RDW) and NLR values in cases with GIM, GA and chronic gastritis, and to show the increased NLR in GIM.

Aims & Methods: 88 patients with GIM and 48 patients with GA and 64 patients with non-atrophic non-metaplastic gastritis were included in the study. NLR and RDW levels were measured in patients and controls.

Results: NLR levels were significantly higher in patients with GIM than in controls ($p < 0.05$). There was no significant difference in NLR levels in patients with GA and controls. There was no significant difference in RDW levels between groups. NLR level was correlated positively with presence of GIM ($p < 0.05$), H.pylori presence in GIM and GA ($p < 0.05$), and menopause ($p < 0.05$). A multiple logistic regression analysis showed the presence of GIM was predictor for elevated NLR ($p < 0.05$). According to the ROC curve analysis, the best cut-off NLR value to differentiate between patients with GIM from GA and/or controls was >2.92 ($p < 0.05$).

Conclusion: NLR is significantly higher in patients with GIM. NLR can be an independent determinant factor for GIM.

References: 1. Eshmuratov A, Nah JC, Kim N, Lee HS, Lee HE, Lee BH, et al. The correlation of endoscopic and histological diagnosis of gastric atrophy. *Dig Dis Sci* 2010;55:1364-75. PMID: 19629687 2. Sato Y, Gonda K, Harada M, Tanisaka Y, Arai S, Mashimo Y. et al. Increased neutrophil-to-lymphocyte ratio is a novel marker for nutrition, inflammation and chemotherapy outcome in patients with locally advanced and metastatic esophageal squamous cell carcinoma. *Biomedical Reports* 2017;7:79-84. PMID: 28685065

Disclosure: We have no conflict of interest

P0009 WITHDRAWN

P0010

AN INFLAMMATORY TUMOUR MICROENVIRONMENT IS ASSOCIATED WITH POOR RESPONSE TO NEO-ADJUVANT CHEMORADIO THERAPY AND POOR PROGNOSIS IN OESOPHAGEAL ADENOCARCINOMA

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Introduction: Oesophageal adenocarcinomas (OAC) are relatively unresponsive to neo-adjuvant chemoradiotherapy (nCRT). The mechanism of a poor response to nCRT is not yet understood. One critical factor in the (non-)responsiveness to nCRT might be an immunosuppressive tumour microenvironment (TME). In this study, TME characteristics associated with a poor response to nCRT in OAC patients were investigated.

Aims & Methods: To study TME characteristics post-nCRT surgical resection specimens from 123 OAC patients and pre-nCRT biopsies from 42 patients were analysed using immunohistochemistry for immune cell subsets. The association between TME parameters and response to nCRT was studied, as well as the association between TME parameters and patient survival. In addition, characteristics in pre-nCRT and post-nCRT samples were compared.

Results: Non-responsive tumours showed a higher immune infiltrate density compared to responsive tumours in post-nCRT tumour samples, with a higher density of CD3+ T-cells ($p < 0.001$), CD8+ T-cells ($p = 0.001$), FOXP3+ T-cells ($p = 0.02$) and CD20+ B-cells ($p = 0.006$) (Table 1). The ratio between the different subsets of immune cells was not different between responders and non-responders. Non-responders showed more frequently PD-L1 expression compared to responders (59% versus 23%, $p < 0.001$). A high CD8 T-cell infiltration was significantly associated with a worse patient survival compared to a low CD8 T-cell infiltration. The PD-L1 status was discordant between pre- and post-nCRT samples in 15 of 40 (38%) patients.

	Responders n=62		Non-responders n=61		p-value
mean CD3+ count/mm2	1324		2370		<0.001
mean CD4+ count/mm2	442		827		<0.001
mean CD8+ count/mm2	641		1126		0.001
mean FOXP3+ count/mm2	182		261		0.024
mean CD20+ count/mm2	416		717		0.006
CD8+/CD3+ ratio	0.51		0.46		0.93
FOXP3+/CD3+ ratio	0.14		0.13		0.10
PD-L1 expression*	negative	46 77%	25 41%		<0.001
	positive	14 23%	36 59%		

[Table 1]

Conclusion: Following results of this study, an 'immune-inflamed phenotype' and an immunosuppressive TME identify OAC patients refractory to nCRT, suggesting that immunotherapy may be a valuable alternative or additional treatment option for this group of patients.

Disclosure: Nothing to disclose

P0011

ANTI-INFLAMMATORY EFFECT OF EV (EXTRACELLULAR VESICLES) ISOLATED FROM *BIFIDOBACTERIUM BREVE* IN RAW264.7 MACROPHAGE

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Introduction: *Bifidobacterium breve* (*B. breve*) secrete extracellular membrane vesicles (EV), which contain DNA, protein, and cell-wall components. EV is involved in microbiota-host cell communications in various biological systems. It was also reported EVs from *B. breve* can prevent intestinal inflammation through the induction of intestinal IL-10-producing Tr1 cells. In this study, we tested whether EV isolated from *B. breve* has an anti-inflammatory effect in LPS-induced inflammation.

Aims & Methods: *B. breve* was isolated from a human fecal sample, and it was cultured over 48 hours at 37°C under anaerobic conditions. After cultivation, the culture medium was centrifuged, subsequently, the supernatant was collected and concentrated. To measure whether the EV affects the viability of the Raw264.7 cell line, WST-1 analysis was used. NO (nitric oxide) concentration involved in immunity and inflammation was investigated in the cell line. ELISA was used to measure the production of inflammatory cytokine.

Results: The anti-inflammatory effect of EV isolated from *B. breve* was confirmed in Raw264.7 cell line. All experiments about EV treatment were under conditions of LPS-stimulation. When the pre-stimulated macrophages were treated with the EV, the concentration of NO, inflammatory factor, was significantly reduced than control. The EV (1ug/ml) treatment group (59.0±3.46 μM/L, p value vs positive = 0.012) had a 13% lower NO value than the positive control group (67.7±8.58 μM/L). It was also significantly reduced the TNF (tumor necrosis factor) level (40%, p value vs positive = 0.0029) of EV (1ug/ml) treatment group under the same conditions. However, IL-6 (interleukin-6) level (165%, p value vs positive = 0) which acts as both the anti-inflammatory factor and pro-inflammatory factor was increased. In this condition, cell viability was not different between EV treatment group and control group.

Conclusion: EV isolated from *B. breve* had an anti-inflammatory effect in the macrophage of inflammatory condition induced by LPS. These results suggested the potential that just EV alone without whole live form probiotics could help suppress the inflammation.

Disclosure: Nothing to disclose

P0012

A RISK-BASED DIAGNOSTIC ALGORITHM OPTIMIZES THE MANAGEMENT OF CAUSTIC INTAKE

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Introduction: Caustic ingestion is a potentially severe condition and identifying patients with a worse prognosis is essential to guide the treatment. Some authors recently proposed the use of computed tomography (CT) as the first test after every caustic intake, instead of endoscopy (1); however, these studies are based on samples from severe patients and their conclusions may not be completely inferred to the general population. An optimal diagnostic algorithm, based on the analysis of the different prognostic markers, would allow to detect severe cases and reduce the number of diagnostic tests.

Aims & Methods:

Aims: 1. To identify risk factors for poor evolution of caustic intake in order to develop a diagnostic algorithm based on these predictive factors.

2. To evaluate its diagnostic accuracy and to compare this algorithm to a CT-based strategy.

Methods: A prospective cohort study was designed to include all patients older than 15 years attended on Clinical University Hospital of Valencia after a caustic intake, between 1995 and 2020.

The main variable is the adverse outcome, defined as any of these three conditions:

- Intensive care unit (ICU) admission.
- Emergency surgery.
- Death.

The intensity of the association of clinical, analytical, endoscopic and radiological variables with the adverse outcome was evaluated; a logistic regression analysis was therefore performed to identify independent risk factors for poor outcome and to develop a diagnostic algorithm based on the risk of poor evolution. Multiple imputation was used to address the missing data.

The diagnostic performance of this algorithm was assessed and finally, the number of tests required by this algorithm were compared with those of a CT-based strategy (1).

Results: 509 cases of caustic ingestion were included during this period. The variables predicting poor outcome were: a high volume intake (>200 ml) or a strong pH substance (OR 3.0, 95%CI 1.6-5.9), oropharyngeal and laryngeal lesions (OR 2.1, 95%CI 1.1-4.1), relative neutrophilia (OR 5.4, 95%CI 3.4-8.6), metabolic acidosis (OR 17.5, 95%CI 10.7-28.5) and the grade of endoscopic injury according to Zargar's grade (OR 5.1, 95%CI 4.0-6.5).

In case of low-volume ingestion of weak caustic (< 200 mL), the risk of adverse outcome, in the absence of oropharyngeal lesions, is 0% in our series. Neutrophilia (≥75%) and acidosis (pH< 7.35) also predict the risk of poor outcome after caustic intake: in their absence, the risk of unfavorable evolution is low (OR 0.0, 95%CI 0.0-0.1), medium if one of them exists (OR 23.3, 95%CI 9.1-59.8) and high if both are present (OR 73.2, 95%CI 28.4-188.6).

The diagnostic algorithm based on these variables has an overall 92.5% sensitivity, 95.4% specificity, 76.5% positive predictive value and 98.8% negative predictive value for any adverse outcome (Table 1).

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
ICU admission	92.1	94.5	71.6	98.8
Surgery	100	86.1	19.8	100
Death	96.4	88.1	33.3	99.8
Any outcome	92.5	95.4	76.5	98.8

[Table 1. Diagnostic accuracy of the algorithm]

According to this algorithm, 46.2% of patients would not require any examination, 53.8% would need a blood test, 11.5% a CT scan and 35.7%, an endoscopy; on the other hand, according to a CT-based strategy, CT would be performed in 100% of patients and endoscopy in 23.6%.

Conclusion: A risk-based diagnostic algorithm can reliably predict the outcome of caustic ingestion and reduce the number of tests of a CT-based strategy.

References: (1) Lancet 2017; 389: 2041-52.

Disclosure: Nothing to disclose

P0013

CRYPTOGENIC ESOPHAGEAL STRICTURES: CAN THE DERMATOLOGISTS HELP US?

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Introduction: Esophageal strictures can be associated with cryptogenic esophagitis, sometimes termed esophagitis dissecans or lymphocytic esophagitis. This endoscopic presentation condition is heterogeneous and associated with alcohol and tobacco consumption, and dermatological conditions, such as lichen planus or auto immune bullous dermatosis. Endoscopic findings include a thickening of the esophageal mucosa, a narrowed esophageal lumen and mucosal sloughing, spontaneously or following a mucosal biopsy. We aimed to assess the prevalence of dermatological conditions in patients with a cryptogenic esophageal strictures.

Aims & Methods: All patients identified with a cryptogenic esophagitis associated with dysphagia revealing an esophageal stricture were identified from a prospective database. These patients were scheduled for a workup including clinical evaluation with a gastroenterologist and a dermatologist, blood tests, skin biopsies, and upper gastrointestinal endoscopy with mucosal biopsies.

Results: Twenty-three patients, of which 14 women (61%), with a median (IQR) age of 67 years (58-80.5) were included. The median time from dysphagia onset was 7 years (4-11.5).

All patients presented with dysphagia at diagnosis and 30% had lost weight. The endoscopic findings were a single esophageal stricture in 56% of the cases, localized in the upper third in 83% of the cases. Mucosal sloughing was described in 26% of the cases and ulcers in 34% cases. Eighty-seven percent of the patients received endoscopic treatment by repeated dilatations for 90% and local steroid injection for 25%. Esophageal biopsies concluded to lichen planus aspect in 30% of the cases, parakeratosis in 17% of the cases, lymphocytic esophagitis in 17%.

For 12 of 23 patients (52% of patients), oral involvement (n = 11), skin lesions (n = 7) or vulvo-anal lesions (n = 8) were found on dermatological examination. Six patients received systemic treatment, based on corticoste-

roids for all patients, immunosuppressive drugs for 2 patients and plasmapheresis for one patient. Skin biopsies concluded to a lichenoid aspect for three patients and inflammatory exocytosis was described for 4 patients. One patient had a positive direct immunofluorescence on skin biopsy, leading to diagnose bullous pemphigoid. This patient also had positive anti-basement membrane antibodies while the anti-BP 180 and 230 antibodies were negative in all patients for whom it was sampled (n = 11).

Conclusion: Cryptogenic esophageal strictures are a challenge to the gastroenterologist because of the poor contribution of mucosal esophageal biopsies and the lack of standardized and effective treatment. In our experience, dermatological evaluation helped in 50% of cases to introduce a systemic treatment leading to reduce the frequency of endoscopic treatments.

Disclosure: Nothing to disclose

P0014

NATURAL HISTORY OF AUTOIMMUNE ATROPHIC GASTRITIS: A RETROSPECTIVE, TERTIARY CENTRE EXPERIENCE FROM A HIGH-RISK AREA FOR GASTRIC CANCER

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Introduction: Autoimmune atrophic gastritis (AAG) is a chronic inflammatory condition that results in a progressive replacement of the corpus parietal cell mass by atrophic and metaplastic mucosa. It is considered a pre-malignant condition due to increased risk of gastric neuroendocrine neoplasms (g-NENs) and gastric adenocarcinomas. Hence, endoscopic surveillance is recommended every 3 to 5 years. However, data on clinical outcomes in histologically confirmed AAG is scarce, particularly in high-risk regions for gastric cancer, as the north of Portugal.

Aims & Methods: To characterize the clinical, analytical, endoscopic and pathological phenotype of patients with AAG and to evaluate the risk of progression of pre-malignant gastric conditions and the occurrence of gastric neoplasia during the follow-up (f-up) by a retrospective identification of adult patients with positive anti-gastric parietal cell (anti-GPC) and/or anti-intrinsic factor (anti-IF) antibodies, from 01/2014 to 08/2019 (n=585) and inclusion of those with histologic findings consistent with AAG.

Results: A total of 145 patients (pts) were included (71.7% female sex) with a mean age of 55.8±15.1 years. 27.6% had another autoimmune disease, 11.9% (14/117) reported a family history of gastric adenocarcinoma and 43.1% (59/137) infection with *H. pylori*. 70.3% showed anti-GPC (+) and 5.5% anti-IF positivity alone; 24.1% showed both autoantibodies (+). At diagnosis, 67.6% had anaemia, 62.8% vitamin B12 deficiency (19.2% PA) and 46.2% iron depletion.

At the first endoscopic evaluation (T-0), gastric body biopsies revealed intestinal metaplasia (IM) in 79.7% and chronic atrophic gastritis (CAG) in the remaining. Antrum biopsies found premalignant conditions in 44.2% (23.9% CAG; 20.3% IM). Gastric dysplasia (g-DYS) was diagnosed in 5 (3.45%) pts (4 low-grade; 1 high-grade dysplasia; up to 22mm). Enterochromaffin like (ECL) cell hyperplasia was found in 9 (6.2%) and ECL dysplasia in 2 (1.4%) pts. 13 g-NENs were diagnosed in 11 (7.6%) pts (most up to 5mm (n=10), all grade 1 (G1) and stage I g-NENs, except for one 13mm g-NEN, G1, stage II, resected by endoscopic submucosal dissection).

Pts had a mean clinical f-up time of 5.06±3.95 years. 84 pts were submitted to endoscopic f-up during a mean time of 4.24±2.87 years. During this period, a significant progression of gastric pre-malignant conditions was not

found. No g-DYS or adenocarcinoma were detected. Overall, 18 g-NENs were detected (up to 7mm; 15 G1, 3 G2; all stage I) among 8 pts, including 13 g-NENs out of 5 patients with g-NEN at T-0. The mean time to g-NEN development was 44.8 months (maximum 81 months). The incidence rate of new g-NENs was 9.7 per 1000 person-years. 4 pts died, none related to AAG.

In bivariate analysis, both ECL hyperplasia (28.6% vs 7.6%, $p=0.012$) and dysplasia (100% vs 7.1%, $p<0.001$) were associated with g-NETs. Pts with ECL hyperplasia had a 4.84 higher OR of developing g-NENs [CI 95% 1.28-18.24]. Male gender (9.8% vs 1.9%, $p=0.033$) and *H. pylori* infection (8.5% vs 1.3%, $p=0.042$) were associated with g-DYS.

Conclusion: ECL hyperplasia and dysplasia were associated with the development of g-NETs, whereas male gender and *H. pylori* infection were associated with gastric dysplasia. Overall, 14.5% of AAG pts developed gastric neoplasms (g-NEN 9.66%; g-DYS 3.45%). All g-NENs and gastric dysplasia were early lesions amenable to endoscopic management. There was no AAG related mortality during the median 5-year f-up time, confirming the overall benign disease course when support treatment and endoscopic follow-up are offered.

Disclosure: Nothing to disclose

P0015

IMMUNE RESPONSE AND MACROPHAGE PHENOTYPE REGULATION IN GASTROESOPHAGEAL REFLUX DISEASE WITH PULMONARY MANIFESTATIONS

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Introduction: Respiratory system inflammation and Th1/Th2 immune response imbalance are the key components of pulmonary manifestations in gastroesophageal reflux disease (pGERD) pathogenesis. Immune response disorders and inflammation depend greatly on the combination of macrophage phenotypes (MPH) in respiratory tract. MPH is specified by the cell microenvironment and one of significant bivalent regulators in alveolar macrophages (AM) phenotypes is surfactant protein D (SP-D). So quantitative and qualitative SP-D analysis is one of the factors influencing macrophage phenotype and plasticity in pGERD patients.

Aims & Methods: This study evaluated pooled data of AM phenotype (AMPH) and plasticity and quantitative/qualitative composition of SP-D in broncho-alveolar lavage (BAL) in pGERD patients as compared to pGERD + asthma and healthy volunteers (HV). Pooled AMPH analysis in patients with pGERD ($n=21$, 44.46 ± 3.52 y.o.), combination of pGERD and asthma ($n=19$, 47.62 ± 4.38 y.o.) and healthy volunteers (HV) ($n=10$, 51.83 ± 3.52 y.o.) included receptor (CD80/CD206) and secretory characteristics (pro-/anti-inflammatory/bivalent M1/M2 cytokines) in AM culture medium assessed by flow cytometry (Beckman Coulter FC500). Quantitative SP-D analysis in BAL was performed by ELISA. Qualitative SP-D oligomeric forms were assessed by western blot analysis with tris-acetate gels (Invitrogen, NuPAGE, #EA03752BOX).

Results: Analysis of AM phenotype by M1/M2 ratio in patients with pGERD, pGERD with asthma vs. HV showed that pooled M1/M2 ratio of AM CD markers and cytokine production was 2.28 and 2.71, 0.86 and 0.93 vs. HV (1.0), respectively. The results indicate AMPH shift to M1 phenotype with predominate M1 plasticity in pGERD and to M2 phenotype with predominant M2 plasticity in pGERD+asthma as compared to HV.

SP-D level in pGERD patients was 2.5 times decreased vs patients with pGERD+asthma (162.31 ± 20.42 ng/ml vs 405.77 ± 38.75 ng/ml, $p<0.05$) and 3.7 times decreased vs. HV (162.31 ± 20.42 ng/ml vs 600.54 ± 46.22 , $p<0.05$).

Qualitative oligomeric SP-D forms analysis showed predominance of monomeric forms both in pGERD and pGERD+asthma vs HV with monomeric and multimeric SP-D oligomers.

Conclusion: There are significant discrepancies in AMPH, AM plasticity and SP-D concentration and qualitative composition in pGERD, combination of pGERD and asthma and healthy volunteers. AMPH shift to M1 vs healthy and maximum decreased SP-D level with predominant monomeric forms are typical for GERD with pulmonary manifestations, whereas shift of AMPH to M2 and less decreasing SP-D level in BALF are specific for pGERD+asthma. Qualitative SP-D analysis showed no significant difference between pGERD and pGERD+asthma, but differed greatly in these groups as compared to healthy volunteers.

Disclosure: Nothing to disclose

P0016

ROLE OF MIRNAS IN GASTRIC ATROPHY, AUTOIMMUNITY AND DISEASE PROGRESSION

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Introduction: MicroRNAs (miRNAs) are small non coding RNAs working as key regulators in biological processes. Their dysregulation seems to be involved in autoimmunity, inflammation and cancer. The autoimmune gastritis (AIG) and the multifocal *H.pylori*-related gastritis (MAG) are pre-neoplastic conditions eventually leading to gastric cancer with a different risk of transformation, being greater for MAG compared to AIG. Furthermore, in AIG the enterochromaffin cells hyperplasia, can further develop into gastric carcinoid, a neuroendocrine tumor (NET).

Aims & Methods: Based on evidence in the literature, we selected five specific miRNAs (miR-21, miR-155, miR-142-3p, miR-146, miR-223), involved in autoimmunity and neoplastic progression, in order to evaluate their tissue expression in chronic atrophic gastritis (AIG and MAG) and to compare their expression in patients without atrophic changes (controls).

We wanted to evaluate, the different expression between AIG and MAG with the aim to investigate their possible pathogenic role in autoimmune etiology. Finally, we analyzed if a different miRNAs expression could correlate with OLGA stages, identifying a possible biomarker of neoplastic progression.

We performed an upper GI endoscopy in all patients with biopsy sampling, with staging by experts pathologists according to the OLGA. We used a qRT-PCR technique (quantified by the Livak method) to determinate the expression of miRNAs. Statistics were performed by the Kolmogorov-Smirnov test and using parametric and non parametric tests.

Results: We studied 10 AIG, 10 MAG and 10 controls.

- Analyzing the expression of each single miRNA among AIG, MAG and controls, a significant difference was obtained for all miRNAs ($p<0.05$).
- Analyzing AIG and controls all miRNAs were overexpressed
- ($p<0.008$), as well as in the comparison between MAG and controls ($p<0.05$). Only miR-155, -142, -223 were significant overexpressed in AIG vs MAG ($p<0.05$).
- No differences were found in miR-21 and miR-146 ($p=ns$).
- We observed a significant statistical difference in the miR-21 expression when comparing controls with all atrophic patients (both AIG and MAG) at early (OLGA I-II) and advanced (OLGA III) atrophic stages ($p<0.0001$).

Conclusion: MiRNA are overexpressed in gastric atrophy with chronic inflammation, assuming their role in the immunity-cancer axis. All miRNAs, excepted miR-21, were overexpressed in AIG compared to MAG. Especially for miR-155, -142, -223 we can hypothesize a pathogenetic role in AIG, as they are involved in the control of Treg-Th17.

Homeostasis loss has already been postulated as a possible pathogenetic event in AIG.

The overexpression of miR-21 in MAG vs AIG could be explained by the greater risk of gastric cancer.

Disclosure: Nothing to disclose

P0017 WITHDRAWN

P0018 WITHDRAWN

P0019 WITHDRAWN

P0020

FECAL MICROBIOTA TRANSPLANTATION RESULTS IN BOTH ENGRAFTMENT AND LOSS OF BACTERIA IN RECIPIENTS

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Introduction: Decreased diversity of the fecal microbiota is recognized as a part of gut dysbiosis [1]. Hence treatments increasing microbial diversity, such as fecal microbiota transplantation (FMT), have attracted much attention in recent years.

In many studies FMT has increased the fecal alpha-diversity, a sign of possible engraftment of new bacteria, which has been correlated to improved clinical outcomes [2]. The loss of bacteria from the gut microbiota caused by the introduction of new bacteria through FMT has not been investigated.

Aims & Methods: The aim of our research was to investigate the engraftment and loss of bacteria caused by FMT.

To investigate this we analysed samples from a previously published placebo-controlled randomized clinical trial investigating the effects of 12 days of 25 daily multidonor FMT capsules treating 52 patients with IBS (Irritable Bowel Syndrome) [3].

We tested fecal samples from baseline, and at 15 days, 1, 3 and 6 months following the commencement of treatment using 16S RNA sequencing. We redid the analysis using Amplicon Sequence Variants (ASVs) instead of (97% clustered) OTUs. The patients were divided into FMT and Placebo responders and non-responders based on the predefined definition of response of at least a 50 points reduction in the IBS-severity symptom score (IBS-SSS) after 3 months. Criteria were composed to define ASVs as present or absent in a group of samples in a manner accounting for (i) differences in numbers of samples in each group and (ii) the differences in the numbers of sequencing reads per sample. An ASV was defined as engraft-

ing when it was present in the Donors, was absent in the patients at baseline and was present in the patients at a following time-point. An ASV was defined as lost when it was present in a group of samples at baseline and not present at a later time-point.

Results: The FMT patients acquired (15 to 18 depending on time-point) ASVs present in the donors while the placebo patients didn't (0 to 1). The FMT group also lost (43 to 66) ASVs at a much higher rate than did the Placebo group (13 to 24 ASVs). The FMT responders and the FMT non-responders acquired similar numbers of ASVs, but the FMT responders seemed to lose ASVs at a higher rate (67 to 101) than the FMT non-responders (35 to 46). Looking at ASVs that were found engrafted at all time-points, *Prevotella copri* accounted for 2 of the 8 ASVs in the FMT group, 7 of the 13 ASVs in the FMT responders and 2 of the 12 ASVs in the FMT non-responders.

Conclusion: FMT induced both engraftment and loss of bacteria in the recipients. In particular *Prevotella copri* had the potential to engraft into the FMT responders' microbiota. Whether the loss or engraftment of certain bacteria are correlated with beneficial clinical effects in IBS patients is still unanswered.

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Disclosure: Nothing to disclose

P0021 WITHDRAWN

P0022

CIRCULATING MICROBIOME SINGATURES IN PATIENTS WITH GASTRIC CANCER

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Introduction: Gastric cancer (GC) is one of the most lethal gastrointestinal malignancies. Up until now there are no reliable biomarkers for early identification of GC patients. Strong evidence suggests mucosal microbiome to play a crucial role in carcinogenesis. Emergic studies shows that microbial DNA can be detected in the blood circulation and may represent the microbiome of distant sites or serve as potential biomarkers of various diseases.

Aims & Methods: In this study we have aimed to detect changes in circulating blood microbiome in gastric cancer patients. Our study was conducted in Department of Gastroenterology of Lithuanian University of Health Sciences, Kaunas Clinics and included a cohort of 31 patients with GC and 41 healthy control (HC) subjects. 16S rRNA gene sequencing of V1-V2 variable regions was used to determine bacterial composition of blood plasma samples.

Results: Taxonomic composition analysis at the phylum level revealed that blood microbiome in both GC patients and HC subjects was predominated by *Proteobacteria*, *Bacteroidetes*, *Actinobacteria* and *Firmicutes*. α -diversity was significantly increased GC patients. Bacterial community structure showed significant clustering between HC and PH patients. Differential abundance analysis revealed *Escherichia/Shigella*, *Peptoniphilus*, *Polynucleobacter* to be associated with gastric cancer. Levels of *Paracoccus* was positively correlated while *Bacteroides*, *Ruminococcus*, *Oscillibacter* were inversely correlated with TNM stage. Random forrests classification between GC and HC based on circulating microbiome profiles yielded an area under receiver operating characteristic curve of 0.7.

Conclusion: Circulating blood microbiota comprises of four main phyla *Proteobacteria*, *Bacteroidetes*, *Actinobacteria* and *Firmicutes*. Circulating microbiome of GC patients is significantly altered in comparison to HC subjects.

Disclosure: Nothing to disclose

P0023

MICROBIOME ANALYSIS OF GASTRIC CANCER TISSUE AT DNA AND RNA LEVELS

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Introduction: Gastric cancer (GC) is still one of the most common and fatal cancers worldwide. The pathogenesis of GC is involved with *Helicobacter pylori* infection, but only 1-2% of those infected develop this tumor. Recent studies have shown that in addition to *H.pylori* in the stomach, there are many other potentially pathogenic bacteria whose composition is altered in GC [1][2].

Aims & Methods: The aim of this study was to perform a microbiome analysis of gastric biopsies at the DNA and RNA levels in GC. In total, 337 samples from 91 individuals were included in this study, 23 of them were control individuals and 68 patients with GC. Biopsies were taken from damaged tumor mucosa and tumor adjacent mucosa at least 5 cm from the tumor tissue. From all biopsies RNA and DNA were extracted. RNA was reverse transcribed into cDNA. V1-V2 region of bacterial 16S rRNA gene from all samples were amplified and sequenced on an Illumina MiSeq platform. To construct sample-similarity matrices abundances of taxonomic ranks in each sample type were used by applying Bray-Curtis algorithm. For significant differences between groups Permutational multivariate analysis of variance (PERMANOVA) and Mann-Whitney test followed by false-discovery rate test were used.

Results: After taxonomic annotation, 10496 phylotypes, belonging to 463 genera and 22 different phyla were identified. No significant differences between tumor and tumor adjacent tissue biopsies both at the DNA and RNA levels were identified. Significant differences were found only in comparison with the control group. We detected 15 and 27 bacteria in GC which significantly differed from the control group at the DNA and RNA levels, respectively. In control group most abundant bacteria made up to 18% at the DNA level and up to 40% at the RNA level. In GC group most abundant bacteria increased till 99% at the DNA level and 100% at the RNA level. The bacterial communities in the tumor tissue biopsies were characterized by decreased richness and heterogeneity (measured by the

Shannon and Simpson indexes) than in control group samples. Some of the bacteria (*Actinomyces*, *Atopobium*, *Prevotella*, *Veillonella*) were present at higher abundance at the DNA level than at the RNA level. *H.pylori* were present in tumor adjacent tissue biopsies at higher abundance compared to tumors tissue biopsies and even more compared to healthy tissue biopsies.

Conclusion: In a microbiome analysis of GC differences were found between tumor tissue biopsies and control group, which differed not only in bacterial composition, but also in number and diversity. An microbiome analysis of GC and control groups at the RNA level revealed more bacteria with less abundance.

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Disclosure: Nothing to disclose

P0024

THE MICROBIOME OF THE ESOPHAGUS, STOMACH AND DUODENUM IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE - PILOT STUDY

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Introduction: These days gastroesophageal reflux disease (GERD) represents one of the significant health problems of western countries as a result of several lifestyle factors. Prolonged GERD leads to esophageal inflammation and significantly increases the risk of Barrett's esophagus (BE) and the subsequent development of esophageal adenocarcinoma (EAC). There is an association between the esophageal microbiome and several esophageal diseases. However, it remains unclear whether the change in microflora leads to esophageal disease, or if this is a side effect of the highly acidic environment created by GERD.

Our pilot study aimed to describe oral bacterial biota in patients with GERD and healthy controls from different parts of the esophagus, stomach and duodenum. Detailed microbiome analysis could contribute to early diagnosis and to the application of effective treatment in patients with GERD.

Aims & Methods: Tissue samples were taken from each patient with biopsy forceps from several sites in the esophagus, stomach and duodenum. From a total of 74 biopsy specimens obtained via endoscopic examination of 2 patients with GERD, 4 with BE, 4 with EAC and 6 healthy controls,

nucleic acid was isolated using the All Prep DNA / RNA / miRNA Universal Kit (Qiagen). The composition of the bacterial community was analyzed by sequencing the 16S rDNA PCR products of the V3-V4 regions on the Illumina MiniSeq platform.

Results: The sequence provided 8,335,646 pair-end reads passing quality filters. To describe the bacterial community richness in the collected samples, their alpha diversity was estimated, calculated using normalized rarefaction values. Specific pathological conditions did not significantly change alpha diversity measures (Shannon's diversity 2.52 Control; 2.48 RE; 2.51 BE; 2.32 EAC); however, there was a trend towards decreased diversity in EAC samples. The relative abundances of the five most abundant phyla in each sample collected were estimated to describe shifts in the bacterial community structure with different conditions. On average, the five most commonly represented bacterial genera were: Firmicutes (39%), Proteobacteria (45%), Bacteroidetes (9%), Actinobacteria (3%), and Fusobacteria (1%). Comparison of bacterial communities made using a non-metric multidimensional scaling (NMDS) plot (based on Jaccard similarity, with 97% identity) shows an apparent clustering of esophagus and stomach/duodenum samples. Distribution of taxonomic abundances showed that esophagus samples were dominated by *Streptococcus* and *Prevotella* with a lower representation of *Veillonella*, as reported previously. On the other hand, we did not observe significant clustering of samples from individual pathological conditions but only an increasing trend in gram-negative taxa (*Fusobacterium*, *Campylobacter*) was found in esophagus samples from RE and BE patients. Further, an increase in taxa *Campylobacter* and *Lactobacillus* taxa was observed in the group of EAC patients.

Conclusion: In our pilot study, we demonstrated the feasibility of a testing procedure in clinical practice. Our findings are consistent with recent studies presenting the predominant colonization of the esophagus with the bacteria *Streptococcus* and *Prevotella* and a lower proportion of *Veillonella*. Due to the small number of patients of the same age in the individual groups tested, we were not able to prove significant clustering in a metagenomic analysis. For this reason, we are currently conducting a more extensive study under physiological and pathological conditions in patients with GERD, whose results will be presented.

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P0025

CHARACTERISTICS OF DONORS FOR FAECAL MICROBIOTA TRANSPLANTATION OF A HIGH-VOLUME STOOL BANK: A 7-YEAR EXPERIENCE

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Introduction: Donor screening is an essential step of the fecal microbiota transplantation (FMT) workflow. Over years, methods of screening have become stricter, based on evolving recommendations, and recruitment have become accordingly more difficult.

Aims & Methods: Our aim is to describe the characteristics of stool donors from the establishment of our FMT centre to date, along with changes in recruitment and screening protocol. All donors pre-screened (investigating their willingness to donate and potential logistical issues) and screened from July 2013 to May 2020 at our FMT centre were included. Our donor screening protocol was first based on available evidence and, from 2016, based on available guidelines. Its last version dates back to 2019, and includes: donor questionnaire; blood and stool testing; questionnaire and rapid stool assay at each donation. Demographics of all included subjects, as well as specific reasons for exclusion, were recorded.

Results: In the study period, five hundred and fifty-two potential donors were evaluated. Of them, 238 were not available to donate because of age out of range, personal or logistic issues. Of the 314 remaining potential donors, 183 failed the clinical questionnaire, mainly because of recent antibiotic use, medical comorbidities, elevated BMI. One-hundred and twenty-one donors underwent blood and stool testing. Of them, 53 individuals were excluded, mainly because of positivity at stool culture or at rapid stool assay. Overall, only 78 of 552 potential donors (14%) were enrolled to donate.

Conclusion: In our FMT centre, only a small rate of potential donors were finally included to donate. Our results suggest that recruitment of stool donors for FMT can be challenging if strict and rigorous screening protocols are followed. Stool donation should be promoted and encouraged among general population, and dedicated incentive to stool donors are advocated.

Disclosure: Nothing to disclose

P0026

GASTROINTESTINAL SYMPTOMS AND OUTCOMES OF HOSPITALISED SARS-COV-2 PATIENTS. A RETROSPECTIVE STUDY FROM A LARGE UNIVERSITY HOSPITAL IN THE WEST MIDLANDS, UK

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a respiratory contagious infectious disease that lead to a global pandemic in a matter of few months. Gastrointestinal (GI) symptoms were reported between 3 to 61% in affected patients [1-5]. The pathogenic mechanism of SARS-CoV-2 is yet to be discovered.

Aims & Methods: This study aimed to look for GI symptoms and outcomes of hospitalised SARS-COV-2 patients. Between 24/01/20 to 13/04/2020, SARS-CoV-2 cases were searched. A case was defined by a positive real time - reverse transcriptase Polymerase Chain Reaction (RT-PCR) for viral RNA of SARS-CoV-2 from nasal swab/sputum. Data was analysed by both IBM SPSS and R statistics software. Covariates of interest were analysed using logistic regression.

Results: 321 patients were identified. Age range was 14 to 104 years. Mean age was 68.95 years. The most commonly admitted patient with the disease was aged 80 years. There were 189 males (58.9%). Caucasian origin represented (77%), while the black, Asian, and minority ethnic (BAME) groups represented 23%. Mean body mass index (BMI) was 24.2 Kg/M². Commonest symptoms were dyspnoea (62.9%), fever (59.1%), and cough (56%). Abnormal chest radiograph was found in (58.6%).

4.3% had history of chronic liver disease and only 1.2% of patients had history of inflammatory bowel disease. At presentation, the gastrointestinal symptoms were reported in 38 patients (11.8%). In more detail; abdominal pain in 15 patients (4.6%), diarrhoea in 14 patients (4%) and nausea and vomiting in 15 patients (4.6%). 44 patients were admitted to intensive care unit (ICU) of these diarrhoea was present in 4.4% of the patients, while nausea, vomiting and abdominal pain were present in 2.2%.

Mean admission time was 10.28 days. The overall mortality was 32.4%. There was significant correlation between increasing age and death (correlation coefficient of 0.330 and P=0.01). Regression analysis revealed that the non-survivors had lower albumin (median of 37, IQR 32.0 to 39.0 g/l) compared to survivors (median of 38, IQR 34.2-41 g/l) (P=0.002). Also, non-survivors had higher CRP levels (median of 129, IQR 51 to 222 mg/l) compared to survivors CRP (median of 61.5, IQR 25.7 to 125 mg/l) (P=0.000). The neutrophil lymphocyte ratio (NLR) was significantly higher in non-survivors (median of 7.2, IQR 4.6 to 13) compared to survivors (median NLR of 5.7, IQR 3 to 9) (P=0.028). However, when the logistic regression analysis was adjusted for age only CRP (P=0.000) and Albumin (P=0.005) were predictive of mortality while the NLR became non-significant (P=0.198) and the age adjustment revealed that NLR was actually increasing with age.

Conclusion: GI symptoms were not commonly reported during the presentation of SARS-CoV-2 patients. The disease had high mortality among hospitalised patients. GI symptoms did not seem to affect requirement for admission to ICU. CRP and albumin could be predictors of mortality.

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Disclosure: Nothing to disclose

P0027

PREDICTIVE FACTORS OF REBLEEDING AFTER ENDOSCOPIC HEMOSTASIS IN THE TREATMENT OF GASTRODUODENAL PEPTIC ULCERS IN JAPANESE PATIENTS

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Introduction: Endoscopic hemostasis is the first treatment for acute upper gastrointestinal (UGI) ulcers, and it can avoid emergency surgery. However, it can be difficult to completely achieve in some patients, and excessive hemorrhage from UGI ulcers can be fatal. Endoscopic hemostasis is carried out for UGI bleeding (Forrest classification Ia, Ib and IIa) with high dose proton pump inhibitors or potassium-competitive acid blocker. Despite improvements in endoscopic hemostasis and pharmacological therapies, UGI ulcers repeatedly bleed in 10% to 20% of patients, and those without early endoscopic reintervention or definitive surgery might be at a high risk for mortality. Therefore, determining which factors are involved in rebleeding after an initial endoscopic hemostasis is extremely important for patients with bleeding UGI ulcers. In addition, understanding the factors that contribute to intractable or insufficient initial endoscopic hemostasis is needed to advance the management of such ulcers.

Aims & Methods: This study aimed to determine the risk factors for intractability to initial endoscopic hemostasis. We analyzed 638 patients who underwent emergency endoscopic hemostasis for bleeding UGI ulcers (Forrest classification Ia, Ib and IIa) within 24 hours of arrival at our hospital between April 2000 and March 2019. We retrospectively documented the patients' backgrounds, and evaluated the ulcer location, size of exposed vessels on the bottom of the ulcer size, and Forrest bleeding patterns. To determine the factors involved in intractability to the initial endoscopic hemostasis, we compared patients whose bleeding UGI ulcers were successfully treated with the hemostasis with those who were intractable.

Results: Durable hemostasis was achieved in 538 patients (84.3 %) by using initial endoscopic procedures. Ninety-six patients (15.0 %) with Forrest types Ia, Ib, and IIa at the second look endoscopy were considered intractable to initial endoscopic hemostasis. Two patients (0.4%) who underwent emergency surgery because of failure to the initial endoscopic hemostasis and three patients (0.4 %) who died right after the initial endoscopic hemostasis. Two patients caused heart failure and one patient caused bleeding death. Multivariate analysis indicated that shock upon admission (odds ratio [OR], 2.47; 95% confidence interval [CI], 1.35 to 4.51), hemoglobin upon admission < 8.0 mg/dl (OR, 1.71; 95% CI, 1.02 to 2.88), serum albumin upon admission < 3.3 g/dL (OR, 2.03; 95% CI, 1.16 to

3.55), exposed vessels with a diameter of ≥ 2 mm on the bottom of ulcer (OR, 2.54; 95% CI, 1.60 to 4.03), and Forrest types Ia (OR, 1.83; 95% CI, 1.04 to 3.23) predicted intractable endoscopic hemostasis.

Conclusion: Shock upon admission, hemoglobin < 8.0 mg/dL, serum albumin < 3.3 g/dL, exposed vessels ≥ 2 mm on the ulcer bottom, and Forrest types Ia were identified as independent risk factors associated with initial intractable endoscopic hemostasis in patients with peptic UGI bleeds. Careful observation after initial endoscopic hemostasis is important for patients at a high risk for incomplete hemostasis.

Disclosure: Nothing to disclose

P0028 WITHDRAWN

P0029

MANAGEMENT OF UPPER GASTROINTESTINAL BLEEDING IN A SWEDISH HOSPITAL: THE USE OF GLASGOW-BLATCHFORD AND ROCKALL SCORES

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Introduction: In Western Europe the yearly incidence of upper gastrointestinal (GI) bleeding is around 0.1%. Mortality is 3-14% per episode(1,2). Scoring systems stratify potential outcomes; the Glasgow-Blatchford score classifies patients as high-risk/low-risk for requiring endoscopic intervention and assists in determining the urgency of endoscopic investigation (3). The Rockall Score (4) includes pre-endoscopic and endoscopic variables to predict mortality. These scores are not widely used in Sweden. **Aims & Methods:** We aimed to assess endoscopic intervention and mortality in patients with upper GI bleeding, and whether the use of scoring systems would have impacted management. Patients who underwent an oesophagogastroduodenoscopy (OGD) at our unit in 2016 were assessed and those with pre- or post-operative ICD10 codes of upper GI bleeding were selected. Demographics, hepatic pathology and comorbidities were documented as well as OGD reports (source of bleeding, interventions and repeat endoscopy during the same admission). Pre-operative Blatchford and Rockall scores were calculated and outcomes were assessed.

Results: We reviewed 2247 OGDs. 680 had bleeding as a suspected or post-operative diagnosis. 208 had verified bleeding on the OGD report. Patients were stratified as Blatchford < 6 points or > 6 points. There was no difference in age (66 vs. 68 years) or heart rate (94 vs. 90). Mean systolic blood pressure and Hb on admission were significantly lower in both patients requiring endoscopic intervention and in those with > 6 points ($p < 0.05$). Patients requiring intervention had an odds ratio of 2.2 (95% CI 1.2-4.1) of having Blatchford > 6 compared to others. All patients had a similar median delay between admission and OGD (1 day); in those with Blatchford > 6 fewer patients suffered longer delays ($p < 0.05$). 16 patients died during the admission; upper GI bleeding (and co-morbidities) was the cause of death in all. Positive predictive value increased with rising Rockall Score (14.7% at 8 points) but X2-testing did not show a significantly increased mortality even at a cut-off of 8 points. At this cut-off, mean systolic BP was lower and heart rate higher on admission than in those patients with Rockall < 8 ($p < 0.05$). At cut-offs of 6 and 4 points, sensitivity increased (81.3% and 100% respectively) but specificity (42.3% and 13.4%) and PPV (10.4% and 8.7%) decreased.

Conclusion: The Blatchford score is a better predictor of outcome than the Rockall score. Patients who would have exceeded the commonly used cut-offs for these scoring systems had deviated clinical markers (blood

pressure, Hb and heart rate) which are almost universally measured at admission. Those patients in our study who would have had a higher Blatchford score were referred for more urgent investigation and intervention, suggesting that these scoring systems may aid in predicting the need for urgent endoscopy and intervention but are not vital for doing so.

	All patients (n=280)	Blatchford > 6 (n=106)	Rockall > 8 (n=10)	Required intervention (n=77)	No intervention (n=131)
Median age (range)	71.5 (21-101)	70.5 (27-101)	84 (61-90)	71 (27-101)	72 (21-94)
Gender M/F	118/90	65/41	4/6	48/29	70/61
Blatchford score (median, range)	6 (0-13)	8 (6-13)	6.5 (1-12)	7 (0-13)	4 (0-12)
Rockall score (median, range)	6 (3-10)	6 (3-10)	9 (9-10)	6 (3-10)	6 (3-9)
Number of patients with melena	93 (44.5%)	54 (50.9%)	3 (30%)	36 (46.8%)	57 (43.5%)
Number of patients with syncope	21 (10%)	14 (13.2%)	2 (20%)	8 (10.4%)	13 (9.9%)
Number of patients with known hepatic disease	21 (10%)	19 (17.9%)	0 (0%)	12 (15.6%)	9 (6.9%)
Number of patients requiring endoscopic intervention (%)	77 (36.8%)	49 (46.2%) *	5 (50%)	-	-
Number of patients with rebleeding (%)	26 (12.4%)	22 (20.7%) **	2 (20%)	19 (24.7%) **	7 (5.3%)
Mortality during admission (%)	16 (5.7%)	13 (12.3%) *	3 (30%)	6 (7.8%)	10 (7.6%)

[Patient characteristics and outcomes (* $p < 0.05$ compared to all other patients)]

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P0030

CLINICAL OUTCOME AND PROGNOSTIC INDICATORS IN SUPER ELDERLY PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING IN A 1,132 JAPANESE PATIENT COHORT

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Introduction: In Japan, the population of over 75 years exceeded 13%, and the population has been rapidly increasing. With the recent technological advances in the field of hemostatic treatments, the prognosis of patients with gastrointestinal (GI) bleeding has been improved. Generally, the clinical outcome in patients receiving antithrombotic therapies with upper GI bleeding (UGIB) have a worse outcome compare to that in those without receiving antithrombotic therapies. However, there have been no large studies regarding prognostic indicators in patients with UGIB over 75 years.

Aims & Methods: The aim of this study was to evaluate the differences in clinical outcomes of patients with UGIB over 75 years (super elderly group) compared with patients under 65 years (non-elderly group) and evaluate the factors related to their prognosis. Medical records of patients who had undergone emergency endoscopy for GI bleeding from Jan/01/2011 to Des/31/2017 were retrospectively reviewed. The severity of GI bleeding was evaluated using the Glasgow-Blatchford (GB) and AIMS65 scores. Patients in whom obvious GI bleeding relapsed and/or presented persistent iron deficiency anemia in spite of emergency endoscopy were considered as having a poor clinical course, while the other cases were defined as those with good clinical course.

Results: A total of 1,132 UGIB patients were consecutively enrolled: 470 patients (41.5%) in the super elderly group and 248 patients (21.9%) in the non-elderly group.

Clinical characteristics: GB and AIMS65 score in the super elderly group were significantly higher compare to the non-elderly group ($P < 0.001$). The number of patients receiving antithrombotic therapy were significantly more in the super elderly group compare to that in the non-elderly group ($P < 0.001$), however antithrombotic therapy did not affect their clinical courses.

Factors associated with clinical course: Multivariate analysis (odds ratio [95% confidence intervals]) showed that GB score was not associated with clinical courses in the non-elderly group, but significantly associated with those in the super elderly group (1.67 [1.07-2.60]). The other factors were no association with their clinical courses in both groups.

Conclusion: The severity of UGIB in super elderly patients was significantly higher compare to that in non-elderly patients. Although antithrombotic therapy has been considered as one of the risk factors for UGIB, there was no association between antithrombotic therapy and clinical course. In super elderly patients with UGIB, the prognostic indicator can be patients' general condition at the time of emergency endoscopy regardless of the patients' background.

Disclosure: Nothing to disclose

P0031

HEMOSUCCUS PANCREATICUS: AN INFREQUENT CAUSE OF LIFE-THREATENING HAEMORRHAGE

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Introduction: Hemosuccus pancreaticus (HP) is a rare but life-threatening cause of upper gastrointestinal bleeding through the main pancreatic duct. This condition most commonly follows pseudoaneurysm formation secondary to acute or chronic pancreatitis. It is still considered a surgical problem but advances in medical therapy may enable clinically stable patients to undergo less-invasive methods.

Aims & Methods: The aim of our study is to highlight the challenges in the diagnosis and management of HP and to formulate a protocol to effectively and safely manage this condition - minimally invasive.

We present a case series of five patients (N=5, three men and two women, mean age 55 yrs) admitted to our unit with gastrointestinal bleeding subsequently found to be HP for the period between 2017-2019y.

Results: HP occurred in 3 patients with chronic and in two with acute alcoholic pancreatitis.

All of the patients presented overt digestive bleeding (two with melena, one with hematochezia and haematemesis, one with hematochezia and one hemorrhagic shock).

All of the patients undergo an initial gastroduodenoscopy and CT angiography.

Selective digestive angiography was done in 4 patients:

Arterial embolization was attempted in one patient. Due to partial recanalization of the vessel and re-bleeding 18 days after first procedure, re-intervention was done with additional embolization.

Placement of nitinol SEMS covering the pseudoaneurysm was done in two patients. Due to the persistence of leakage to pseudoaneurysm, a second stent graft was implanted in one of the patients.

In one of the patients the angiography was only diagnostic.

ERCP with pancreatic duct stenting and tamponade was performed in two patients. In one of the patients ERCP was combined with angiography and self-expandable stent placement.

None of the patients required surgical treatment.

Technical and long-term clinical success was achieved in 75% of the patients.

There was one death due to multiple organ failure and hemorrhagic shock.

Conclusion: Although the early diagnosis of HP is challenging, use of appropriate diagnostic studies plays a significant role in reducing mortality and morbidity. We recommend an interventional procedure for the initial treatment of HP, and feel that surgical treatment should only be considered when angiography shows no abnormal findings, when ERCP with stent placement is not suitable option, or when the interventional therapy is not successful.

Disclosure: Nothing to disclose

P0032

INCIDENCE, PREDICTIVE FACTORS AND OUTCOMES OF NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: A PROSPECTIVE MULTICENTER POPULATION-BASED STUDY FROM HUNGARY

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Introduction: Acute upper gastrointestinal (GI) bleeding is associated with significant morbidity and mortality.

Aims & Methods: Our aim was to evaluate characteristics and prognostic factors in the management of acute upper GI bleeding in a large multi-center study from Hungary. The present prospective one-year study involved six major community hospitals in Western Hungary covering a population of 1,263,365 persons in 2016. Data collection included demographic characteristics, vital signs at admission, comorbidities, medications, time to hospital admission and endoscopy, laboratory results, endoscopic management, including endoscopic therapy and second look endoscopy, risk assessment using Glasgow-Blatchford Score (GBS), Rockall Score (RS) and the American Society of Anesthesiologists (ASA) Physical Status Score, transfusion requirements, length of hospital stay and mortality.

Results: 688 cases (incl. 117 in-hospital cases) of acute upper non-variceal GI bleeding were registered, resulting an estimated incidence rate of 54.42 (CI95% 50.5-58.6) per 100,000 population per year in Western Hungary. Time from symptom onset to presentation at the Emergency Department (ER) was < 6 hours in 35.9% and < 12 hours in 52.7% of the cases. Time from hospitalization to endoscopy was < 6 hours in 55.7% and < 12h in 71.8%. Frequent diagnoses were duodenal ulcer (20.6%), gastric ulcer (19.0%), gastroesophageal reflux disease (GERD) (11.1%), erosive gastritis/duodenitis (9.9%) and Mallory-Weiss syndrome (8.2%), malignancy (4.0%) and arteriovenous malformation (AVM) (3.8%). Therapeutic intervention on initial endoscopy was performed in 37.1%, while 35.9% of patients required second look endoscopy. Intravenous proton-pump inhibitor (PPI) was applied in 78.8%, while blood transfusion was given to 65.7% of the patients. Hospitalization stay exceeded 7 days in 50.3%, and 5.3% of the patients required surgery. Mortality was 11.6% among patients with bleeding episode presenting outside the hospital, while the overall mortality rate (including in-hospital bleedings) was 13.5%. Longer time to presentation at the ER predicted transfusion requirements ($p=0.038$), while weekend presentation was associated with transfusion ($p=0.047$), surgery ($p=0.016$) and mortality ($p=0.021$). Presentation with vegetative symptoms at admission (i.e. tachycardia, hypotension or syncope) was associated with increased transfusion needs ($p<0.001$), longer in-hospital stay ($p<0.001$) and mortality ($p=0.017$). Patients on anticoagulant, antithrombotic or non-steroidal anti-inflammatory drug (NSAID) medications had higher transfusion needs ($p<0.001$) and longer in-hospital stay ($p=0.004$), but no increased mortality ($p=0.571$). The GBS was predictive of transfusion (AUC: 0.82; cut-off: GBS >7points; sensitivity: 71.9% specificity: 78%), while mortality was strongly associated with the post-endoscopic RS (AUC: 0.75; cut-off: RS >5points; sensitivity: 68.8% specificity: 68.9%). Presence of comor-

bidity and ASA stage correlated with transfusion requirements (ASA 1-2 vs. ASA 3-4: OR 2.9, CI95% 2.1-4.1; $p<0.001$), endoscopic intervention (OR 1.4, CI95% 1.1-1.9; $p=0.033$), mortality (OR 9.0, CI95% 4.7-17.2; $p<0.001$) and hospitalization length ($p<0.001$).

Conclusion: Incidence rates of acute upper GI bleeding in Western Hungary are in line with international trends. The ASA-score, GBS and RS predicted outcomes and transfusion requirements. We observed higher mortality rates, which can partially be explained by the high comorbidity rates in this population, but warrant optimization of the management of acute non-variceal upper GI bleeding.

Disclosure: Nothing to disclose

P0033

INCIDENCE, PREDICTIVE FACTORS AND OUTCOMES OF VARICEAL UPPER GASTROINTESTINAL BLEEDING - A PROSPECTIVE MULTICENTER POPULATION-BASED STUDY FROM HUNGARY

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Introduction: Acute variceal gastrointestinal (GI) bleeding is associated with significant morbidity and mortality.

Aims & Methods: Our aim was to evaluate characteristics and prognostic factors in the management of acute upper GI bleeding in a large multi-center study from Hungary. The present prospective one-year study involving six major community hospitals in Western Hungary covering a population of 1,263,365 persons in 2016. Data collection included demographic characteristics, vital signs at admission, comorbidities, medications, time to hospital admission and endoscopy, laboratory results, endoscopic management, including endoscopic therapy and second look endoscopy, risk assessment using Glasgow-Blatchford Score (GBS), Rockall Score (RS) and the American Society of Anesthesiologists (ASA) Physical Status Score, transfusion requirements, length of hospital stay and mortality.

Results: 108 cases of acute variceal GI bleeding were registered, providing an estimated incidence rate of 8.54 (CI95% 7.08-10.32) per 100,000 population per year in Western Hungary. Time from symptom onset to presentation at Emergency Department (ER) was < 6 hours in 41.4%, and < 12 hours in 64.6% ($n=99$). Time from hospitalization to endoscopy was < 6 hours in 66.7%, and < 12h in 81.5%. Endoscopy revealed grade 3-4 varices in 63% of patients according to the Paquet's classification of varices. Endoscopic therapeutic intervention was performed in 57.4%, and 38.0% of patients required second look endoscopy. On initial endoscopy, 39.8% of patients were treated with sclerotherapy, 18.5% had ligation and 5.6% balloon tamponade. 76.9% of the patients required blood transfusion. Hospitalization length exceeded 7 days in 45.4% of the patients. Mortality was 18.2% among patients with bleeding episode presenting outside the hospital, while the overall mortality rate (including in-hospital bleedings) reached 24.1%. There was no significant difference in mortality or transfusion requirements based on prehospital time or weekend management

($p=NS$). Presentation of vegetative symptoms at admission (i.e. tachycardia, hypotension or syncope) was associated with increased rates of transfusion ($p=0.003$). The Paquet's grade of varices was correlated with the transfusion needs ($p=0.036$), endoscopic therapy ($p<0.001$), and showed similar trend for mortality ($p=NS$). The increased international normalized ratio (INR) and creatinin levels were associated with mortality ($p=0.001$ and $p=0.002$). The GBS best predicted transfusion requirements (AUC: 0.793; cut-off: GBS >8 points; sensitivity: 72.3% specificity: 76%). The frequency of known ETOH dependency and systemic comorbidity was 84.3% and 98.1% in this population. The patients' ASA stage was associated with transfusion requirements (ASA 1-2 vs. ASA 3-4: OR 7.6, CI95% 2.7-21.6; $p<0.001$), endoscopic intervention (OR 12.6, CI95% 3.4-46.5; $p=0.033$), and showed similar trend with mortality (OR 3.6, CI95% 0.8-16.7; $p<0.095$).

Conclusion: Incidence rates of acute variceal GI bleeding in Western Hungary are high. The ASA-score, GBS predicted outcomes and transfusion requirements. Although comorbidities are very high in this population, the observed high mortality rates, coupled with relatively low rates of endoscopic ligation warrant optimization of management strategies in acute variceal GI bleeding.

Disclosure: Nothing to disclose

P0034

POSITIVE WHITE NIPPLE SIGN ON ESOPHAGEAL VARICES - PETTY OR EXIGENT!

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Introduction: During endoscopy variceal haemorrhage is identified when we see active bleeding from the varices. But majority of the times active bleeding has ceased when we introduce the scope. So, all endoscopists should be well versed with identifying the signs of recent variceal haemorrhage.

The most commonly seen stigmata are red color signs, including red wale marks (longitudinal red streaks on varices that resemble red corduroy wales), cherry red spots, and hematocystic spots (raised discrete red spots on the surface of varices that appear as blood blisters).

A less commonly recognized stigma of recent variceal haemorrhage is a white nipple-like projection from a varix into the esophageal lumen. This is a platelet-fibrin plug. It is referred to as the 'white nipple sign' and is a stigma of a site of recent bleeding. Recognition of this stigma of recent bleeding is necessary to manage that varix endoscopically to prevent further variceal bleeding or intra procedural bleeding and its incipient complications. This sign is not well described in literature and its importance to endoscopists treating esophageal varices still not clear.

Our experience with this sign, recognizing it on endoscopy and dealing with it differently than those cases without the white nipple sign has been the aim of our retrospective analysis. It will definitely be useful to shed light on this important but no much-discussed perspective of esophageal variceal management.

Aims & Methods: **Aim:** To assess if White Nipple Sign on esophageal varices is petty (no prognostic Significance) Or Exigent (Mandates more attention).

Methods: 2601 patients from 2008 to January 2020 with variceal bleed. Management protocol: Glue injection GOV1, GOV 2 and IGV1. 0.5ml glue + 1.5ml to 3ml distilled water. Esophageal varices - EVL. Thoroughly looked for positive white nipple sign. Varix distal to it injected with glue. First band applied on varix with nipple using a special technique.

If active spurt from nipple. EVL performed. If Severe bleeding - identify site. Tamponade with cap. Still not localized- endotracheal intubation and EVL. Banding fails again, inject cyanoacrylate glue just below spurt, then in it. Fully covered Denis Ella stent if everything fails. Repeat endoscopy after 24 hours, remove stent and treat varices.

Results: Total - 2601. Timing of endoscopy- 4-8 hours. Positive White Nipple sign- 631(24.3%).

Blood in stomach- 1124 (43.2%), Nipple sign in this group- 575 (51.2%), No blood in stomach- 1477 (56.8%), Nipple sign in this group - 56 (4.9%). Active spurt from nipple- 137 /631 (21.7%), Endotracheal Intubation- 39 (28.4%), Aspiration -12 (8.8%), Successful EVL - 594 (94.1%), EVL Unsuccessful needing Glue Injections - 35 (5.5%).

Persistent Bleed - 2 (0.3%), Denis Ella FCSEMS 2 (0.3%). Mortality - 3 (0.5%).

Conclusion: White Nipple Sign is not only a predictor of recent bleed, but it signifies significant bleed with increase morbidity and mortality and has to be managed differently with more caution and with specific strategy. Not petty but exigent!

Disclosure: Nothing to disclose

P0035

NO DIFFERENCE BETWEEN ORAL AND INTRAVENOUS PROTON PUMP INHIBITORS FOR BLEEDING PEPTIC ULCERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Current guidelines recommend intravenous proton pump inhibitor therapy in peptic ulcer bleeding. We aimed to compare the efficacy of oral to intravenous administration of proton pump inhibitors (PPI) in peptic ulcer bleeding.

Aims & Methods: We performed a systematic search in PubMed, Cochrane, Embase, Scopus databases for randomized controlled trials which compared the outcomes of oral PPI therapy to that of intravenous PPI therapy for bleeding peptic ulcers. The primary outcome was 30-day mortality. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for dichotomous outcomes, while weighted mean differences (WMD) with CI were calculated for continuous outcomes in meta-analysis. The protocol of the study was registered a priori onto PROSPERO.

Results: A total of 13 RCT reported 1751 peptic ulcer patients, 881 and 870 of which were in the control and intervention groups, respectively. There were no statistically significant differences between treatments regarding 30-day mortality (OR=0.72, CI, 0.29-1.76); 30-day rebleeding rate (OR, 0.91, CI, 0.59-1.38); length of hospital stay (WMD = -0.34 days, CI: -1.17-0.49); transfusion requirements (WMD = -0.05 PRBC unit, CI: -0.28-0.18); need for surgery (OR = 0.91, CI: 0.40-2.07); further endoscopic therapy (OR = 1.04, CI: 0.56-1.93); and need for re-endoscopy (OR = 0.83, CI: 0.51-1.33). Heterogeneity was negligible in all analysis, except for that on the length of hospitalization ($I^2=81.2\%$, $p<0.001$).

Conclusion: Recent evidence suggests that the oral administration of PPIs is not worse than the currently recommended intravenous PPI treatment in bleeding peptic ulcers after endoscopic assessment, warranting guideline revision.

Disclosure: Nothing to disclose

P0036

UPPER GI BLEEDING IN COVID-19 PATIENTS: CHARACTERISTICS AND MANAGEMENT IN A MULTICENTER EXPERIENCE FROM NORTHERN ITALY

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Introduction: Outbreak of the novel SARS-CoV-2 infection, leading to coronavirus disease 2019 (COVID-19) has been declared an official pandemic by WHO on March 11, 2020. COVID-19 patients have an increased susceptibility to develop thrombotic complications, and therefore thromboprophylaxis is routinely administered. The widespread of anticoagulant treatment and the exposure to stress ulcer risk may increase the occurrence of upper gastrointestinal bleeding (UGIB). Timing of upper GI endoscopy should be carefully evaluated given the risk of respiratory worsening in non-intensive care unit (ICU) patients.

Aims & Methods: To retrospectively evaluate the medical and endoscopic management of UGIB in non-ICU COVID-19 patients referred to eight COVID Hub Centers from Northern Italy. COVID-19 inpatients (positive nasopharyngeal swab or bronchoalveolar lavage) older than 18 yrs with overt sign of UGIB were enrolled in the study in the period from March 5th to April 30th. Demographic and clinical characteristics at admission were evaluated. Type of anticoagulant and/or antiplatelet therapy were acquired. Severity of COVID-19 pneumonia was classified according to the type of oxygen support. Glasgow Blatchford score was calculated at onset of signs of GI bleeding. Timing between onset of signs of GI bleeding and execution, if performed, of upper GI endoscopy was evaluated. Endoscopic characteristics and outcome of patients were evaluated overall or according to the execution or not of an upper GI endoscopy before and after 24 hr. Chi-square test with Fisher test and Mann-Whitney test were used when appropriate.

Results: 23 patients (18 male; 75 yrs; IQR 64-78) were included in the study. Antiplatelet therapy was present in 7/23 patients whereas 18/23 (78%) were on anticoagulant therapy before or during hospital stay (35% on prophylactic therapy and 44% in full dose anticoagulant) and 65% of them had two or more comorbidities (78% hypertension or chronic heart disease, 48% diabetes and 9% cirrhosis). 69% of patients had a significant respiratory involvement (high flow oxygen or non-invasive positive pressure support). Signs of upper GI bleeding appeared in a median time of 4 days (0.6-7) during hospital stay being presence of tarry stool the most common finding (52%). In 11 patients (48%) upper GI endoscopy was performed within 24 hr (4 had haematemesis), whereas it was not performed because of complete resolution of bleeding with medical management in 4 patients, and because of severe respiratory worsening in one. Peptic ulcer was the most common finding (8/18) followed by erosive or haem-

orrhagic gastritis (4/18), Mallory-Weiss or Dieulafoy lesion (4/18) and variceal bleeding (1/18). Endoscopic treatment (adrenaline injection + clips in 5 and cyanoacrylate injection in one) was necessary in 6/18 patients. Mortality rate was 21.7%. Mortality (2 vs 3 patients) and rebleeding (2 vs 1 episodes) were not different between patients having upper GI endoscopy before or after 24 hr/not performed. Need of endoscopic treatment was more common in patients in which upper GI endoscopy was performed before 24 hr (6 vs 1 patients, p=0.02) although Glasgow Blatchford score was similar between the two groups (13;12-16 vs 12;9-15).

Conclusion: Upper GI bleeding is not a common complication in COVID-19 patients although the widespread of thromboprophylactic therapy, and peptic ulcer disease is the most common finding. Conservative management with optimization of medical therapy and delay of endoscopy could be an option in patients that are at risk of respiratory complications.

Disclosure: Nothing to disclose

P0037

USE OF A MACHINE LEARNING ALGORITHM TO PREDICT REBLEEDING AND MORTALITY FOR ESOPHAGEAL VARICEAL BLEEDING IN CIRRHOTIC PATIENTS

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Introduction: Esophageal variceal bleeding (EVV) is one of the most common complications of cirrhosis. Its mortality rates range around 15%-20% in the first episode. Given EVVs high rates, identifying patients with a high chance to survive is paramount in order to allocate resources into treatment with accuracy.

Aims & Methods: The purpose of this study is to use a machine learning algorithm to predict rebleeding and mortality for EVV in cirrhotic patients and to analyze its accuracy.

A historical cohort study was conducted, analyzing data from hospital charts from Jan 2010 to Dec 2016. Patients were found by searching every use of terlipresin in the period. Paper and electronic medical charts were hand-analyzed. Patients over 18 years old with laboratory and imaging data supporting the diagnosis of cirrhosis and with a definitive diagnosis of EVV were included.

This analysis used data from 74 cirrhotic patients, taking into account 36 variables, which had EVV as a complication. The preliminary analysis of the study was Pearson Correlation, which compared the 36 variables in study with the outcomes of death and rebleeding. This was in order to verify the linear correlation strength, positive or negative.

When Artificial Intelligence (AI) was applied, an Artificial Neural Network (ANN) was utilized to recognize patterns of the outcomes through supervised learning. The results were analyzed based on a confusion matrix, which presented the probabilities of the Positive Predictive Value, Negative Predictive Value, Sensitivity, Specificity and Network Accuracy. A Receiver Operating Characteristic (ROC) curve analysis was then performed.

Results: Electronic search retrieved 177 hospital admissions with use of terlipresin. 101 were due to EVV. All-cause mortality was 36%, 41.5% and 50.4% for 30-, 90- and 365-day, respectively. Mean age was 56 years-old, 79% were male. Most common cause of cirrhosis was alcohol abuse, followed by hepatitis C.

The Pearson Correlation analysis showed the variables have values of linear correlation ranging from -0.34 to 0.30 to mortality and -0.31 to 0.21 to rebleeding. Both values represent weak correlations with the outcomes. Thus, it is notably difficult to define which variables are the ones with major leverage on the outcomes. Ergo, the use of AI could be a key-tool to identify the patterns in such a complex data-evolved situation.

For patients who had a mortality outcome, the specificity value shows that the ANN was able to identify 95.0% of them. The predictive value shows when the ANN predicted mortality, 95.0% of the patients did indeed perish. The overall accuracy was 97.4% and the Area Under the curve ROC (AUROC) was 0.993, which demonstrates a high performance of the network.

For patients who had a rebleeding outcome, the specificity value shows that the ANN was able to identify 66.7% of them. The predictive value shows when the ANN predicted rebleeding, 100% of the patients did indeed rebleed. The overall accuracy was 97.4% and the AUROC was 0.942.

Conclusion: The ANN could more accurately predict mortality by EVB when compared with two other assessment tools, CLIF-SOFA and MELD Score. The literature has already reported that the CLIF-SOFA has better predictive characteristics than the MELD Score. The AUROC of the CLIF-SOFA found in the literature for the outcome death was 0.943 and the AUROC of the MELD score was 0.80. While, the AUROC of the ANN was 0.993. Therefore, Machine Learning could be a useful tool in order to improve clinical practice, perhaps outperforming the current tools.

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Disclosure: Nothing to disclose

P0038

HEMOSPRAY IN THE TREATMENT OF VARICEAL BLEEDS: OUTCOMES FROM THE INTERNATIONAL HEMOSPRAY REGISTRY

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Introduction: Early treatment for variceal bleeding is recommended within 12 hours to improve outcomes. Endoscopic therapy in acute variceal bleeding can be technically difficult and is not always successful and therefore a bridge is sometimes required towards definitive endoscopic therapy or Trans jugular intrahepatic portosystemic shunt (TIPS). Hemospray (Cook Medical, North Carolina, USA) is an endoscopic haemostatic powder for Gastrointestinal (GI) bleeding.

The aim of this study was to look at outcomes in patients with upper gastrointestinal bleeds (UGIB's) secondary to varices.

Aims & Methods: Data was collected prospectively (January 2016- November 2019) from 16 centres in the USA, UK, Germany, France and Spain. Hemospray was used during emergency endoscopy for a variceal UGIB as a monotherapy, dual therapy with standard haemostatic techniques or rescue therapy once standard methods have failed. Haemostasis was defined as cessation of bleeding within 5 minutes of hemospray application. Rebleeding was defined as a sustained drop in Hb (>2g/l), haematemesis or melaena with haemodynamic instability following index endoscopy.

Results: 12 patients had Hemospray treatment following a variceal upper GI bleed (10 males, 2 female). 10 were oesophageal varices and 2 gastric varices. The median Rockall score was 8 (IQR, 7-8). The median Blatchford score was 15 (IQR, 13-17).

There was an immediate haemostasis rate of 75%. There were no rebleeds following treatment with Hemospray. 4 patients were treated with Hemospray monotherapy, 3 with combination therapy and 5 with rescue therapy (table 1). Hemospray was always given after oesophageal banding or injection sclerotherapy in the combination/rescue therapy cohorts. 4/9 patients died within 7 days, 3 out of these 4 patients did not achieve initial haemostasis with Hemospray.

	Monotherapy (n=4)	Combination (n=3)	Rescue (n=5)
Median Blatchford score	15 (IQR, 14-16)	15 (IQR, 8-17)	12 (IQR, 11-14)
Median Rockall score	8 (IQR, 8-9)	8 (IQR, 6-9)	8 (IQR, 7-8)
Haemostasis (%)	3/4 (75%)	2/3 (66%)	4/5 (80%)
Rockall 7 and 8 predicted re-bleeding rate 25-40%			
Re-bleed	0	0	0
Rockall 8 predicted mortality rate 40-45%			
7-day mortality (%)	1/3 (33%)	2/3 (66%)	1/3 (33%)

[Table 1: Outcomes in the Hemospray subgroups]

Conclusion: The outcomes from the registry showed an immediate haemostasis rate of 75% in variceal UGIBs following treatment with Hemospray. In those cohort of patients there is no re-bleeding. This suggests that Hemospray may play a potential role as a bridging therapy in variceal bleeds which are difficult to control, towards repeat definitive endoscopic therapy or TIPS. Larger trials are required to validate these results.

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P0039

PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING AND PREVIOUS USE OF ANRITHROMBOTIC DRUGS HAVE LESS NEED FOR ENDOSCOPIC THERAPY

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Introduction: Upper gastrointestinal bleeding (UGIB) remains a significant cause of hospital admission with changing epidemiology: aging population, with multiple comorbidities and increased use of antithrombotic (AT) drugs. AT drugs are a recognized risk factor for UGIB (1); however, few studies have evaluated their effects on patient outcomes with controversial results. Previous studies show no differences (2,3) or a higher need (4) for endoscopic therapy (ET) in AT vs. non-AT (NAT) users in non-variceal UGIB. Gao et al. showed more active bleeding in AT users (5) whereas Teles-Sampaio et al. found no differences (2).

Aims & Methods: The aim of our study is to evaluate the effect of AT use on relevant outcomes of patients with UGIB.

This was a prospective study on consecutive UGIB patients (variceal and non-variceal) treated in Virgen de las Nieves University Hospital (2013-2019). All patients underwent upper endoscopy. We considered AT users all patients on antiplatelets (low dose aspirin, thienopyrimidines) and/or anticoagulants (vitamin-K antagonist, direct-acting anticoagulants, heparin). Information regarding clinical, biochemical data and procedures was collected. Documented clinical outcomes were in-hospital and delayed (6-months) mortality, rebleeding and delayed (6-months) hemorrhagic and cardiovascular events. Descriptive, bivariate and multivariate logistic regression analysis was carried out.

Results: 698 UGIB patients were included (63.6% males), 258 (37%) were taking AT drugs (161 antiplatelets, 115 anticoagulants) at presentation. AT differed from NAT group in age (72vs.60;p< 0.001), comorbidities (90.7%vs.45.7%;p<0.001), ASA classification (3.05vs.2.49;p<0.001), AIMS65

score (1.77vs.1.18;p< 0.001), GB score (11.09vs.10.08;p=0.001), heart rate (86.96vs.91.35;p=0.018), hemoglobin levels (9.19vs.9.64;p=0.027), variceal etiology (9.3%vs.22.5%;p< 0.001), active bleeding in endoscopy (25.2%vs.33.2%;p=0.027), need for ET (33.3%vs.43.6%;p=0.007) and in-hospital complications (19.8%vs.13.4%;p=0.026). There were no significant differences in gender, systolic blood pressure, non-variceal etiology, rebleeding (7.8%vs.9.6%;p=n.s), need for interventional radiology or surgery (2.3%vs.4.8%;p=n.s), blood transfusions, hospital stay and acute mortality (8.5%vs.10%;p=n.s).

Analyzing the cause of death between AT and NAT groups, acute mortality related to UGIB was 3.5% vs.6.1 % (p=n.s) and to another cause 4.7% vs.3.9% (p=n.s), respectively.

Regarding of delayed events, patients on anticoagulants had more cardiovascular ones (26.1%vs.14.6%; p=0.002) with no differences found in antiplatelets users. No differences were found regarding hemorrhagic events and mortality in AT users.

After adjustment for age and comorbidities, independent predictors for need for endoscopic therapy were AT use (OR 0.595;95%CI 0.40-0.87;p=0.045), active bleeding (OR 15.56;95%CI 9.18-26.38;p< 0.001), variceal bleeding (OR 3.18;95%CI 1.46-6.95;p=0.004),and GB score (OR 1.10; 95%CI 1.01-1.20,p=0.026).

Conclusion: Despite being older, with higher ASA, GB and AIMS65 score, lower hemoglobin levels at admission, and more comorbidities as well as in-hospital complications; patients who have UGIB and take AT drugs have lower heart rate, active bleeding in endoscopy and need for endoscopic therapy compared with non-AT users. Both had similar rates of rebleeding, need for surgery or interventional radiology, transfusions, hospital stay and acute mortality. Importantly, we also found that the need for endoscopic therapy was lower in AT users, even after adjusting for potential confounding factors, acting as a protective factor.

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Disclosure: Nothing to disclose

P0040

AN ANALYSIS OF THE MORTALITY IN PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING AND NO THERAPY APPLIED IN THE INDEX ENDOSCOPY

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Introduction: Upper gastrointestinal bleeding (UGIB) is a true emergency, associated with significant morbidity, mortality and healthcare costs. The basis of the management nowadays are hemodynamic stabilization and performance of an upper endoscopy within 24 hours after presentation.

Criteria for endoscopic therapy in UGIB has been well established, especially for ulcer related bleeding. However, the rate of endoscopic hemostasis in UGIB patients undergoing endoscopy is variable between series, ranging from 20% to 40% (1,2).

Aims & Methods: Our aim was to analyze mortality in patients undergoing an upper endoscopy because of upper GI bleeding, with no hemostatic treatment applied, causes and improvement strategies.

We use data from a prospective database including consecutive UGIB patients treated in "Virgen de las Nieves" University Hospital from January 2013 to September 2017. All patients underwent upper endoscopy. Information regarding clinical and biochemical data and procedures was collected. Documented clinical outcomes were rebleeding, in-hospital mortality (distinguishing between bleeding related death and due to another event) and delayed (6-months) mortality. Descriptive, inferential and multivariate logistic regression analysis was carried out.

Results: 638 patients (66.1% male) underwent upper endoscopy within 24 hours; 249 (39%) received endoscopic hemostasis, whereas 389 (61%) did not. Active bleeding was present in 6.9% of patients who did not receive endoscopic hemostasis. Mortality in this last group was 5.9%, compared to 14.5% among the patients who received endoscopic therapy ($p < 0.0001$; OR 2.69; CI 95% 1.55-4.66). Among the patients who did not received endoscopic therapy, 13 (3.3%) had a bleeding-related death and 9 (2.3%) died because of previous comorbidities. Within the patients who did not received endoscopic therapy and had a bleeding-related death, causes were esophageal varices (5, two of them had esophageal ulcer too), obscure origin GI bleeding (4), peptic ulcer (3) and neoplasm (1).

Logistic regression showed that independent predictors for in-hospital mortality in UGIB patients who did not received endoscopic therapy were esophageal varices (OR 5.53; CI95% 1.43-21.39; $p = 0.013$), obscure origin GI bleeding (OR 4.83; CI95% 1.11-20.97; $p < 0.036$), esophageal ulcer (OR 16.6; CI95% 2.01-131.93; $p = 0.008$) and a MAP(ASH) score above 2 (OR 1.79; CI95% 1.33-2.42; $p < 0.0001$).

Conclusion: In-hospital mortality in UGIB patients is lower in those who did not receive endoscopic treatment, due to less severe bleeding. However, 5.9% of these patients died, and 3.3% had a bleeding related death. In this group, the most usual cause of death was variceal bleeding, followed by occult GI bleeding that, along with esophageal ulcers and a MAP(ASH) score above 2 were independent risk factors for mortality.

In conclusion, we should lower the threshold to apply hemostatic treatment in patients in whom an UGIB is suspected and we found small varices or varices without bleeding stigmata, as well as with esophageal ulcers; especially if they have a MAP(ASH) score greater than 2.

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Disclosure: The authors have no conflict of interest. This abstract has been previously presented at national meeting.

P0041

ADJUVANT EFFECT OF NEW HEMOSTATIC SPRAY 'NEXPOWDER' ON CONVENTIONAL ENDOSCOPIC TREATMENT IN MANAGING NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: A PROSPECTIVE, MULTI-CENTER, RANDOMIZED CONTROLLED TRIAL

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Introduction: Nexpowder (Nextbiomedical CO., Incheon, South Korea) is a newly developed endoscopic hemostatic powder generating gelation effect on bleeding focus.

Aims & Methods: This study was to evaluate adjuvant effect of Nexpowder though comparing acute and subacute re-bleeding rates between Nexpowder with conventional endoscopic therapy (N+CET, study) group vs conventional endoscopic treatment only (CET, control) group in patients with acute non-variceal upper gastrointestinal bleeding (UGIB).

This prospective, multicenter, and randomized trial conducted from March 2019 to March 2020 in Korea. Consecutive patients (>18 years) with acute UGIB (Forrest classification Ia, Ib, and IIa) who achieved immediate hemostasis through CET were randomized 1:1 to N+CET group or CET only group. Primary outcomes were defined as re-bleeding rate in 3 days and 30 days after therapy and secondary outcomes were safety profiles for Nexpowder.

Results: After exclusion of ineligible criteria, total of 141 patients were randomized into N-CET (n=71) vs CET only (n=70) group. Baseline characteristics including age (study vs control: 63.7 ± 14.0 vs 63.6 ± 14.7 , $p = 0.6$), female proportion (15(21.1%) vs 21(30.0%), $p = 0.3$), anticoagulant use history (16(22.5%) vs 20(28.6%)), $p = 0.5$) were not statistically different between groups. Main reason of bleeding (study vs control: peptic ulcer, 68(95.8%) vs 61(87.1%), $p = 0.2$), initial bleeding control method before randomization (Argon plasma coagulation, 43(60.6%) vs 44(62.9%), $p = 0.9$), Glasgow-Blatchford bleeding score (10.21 ± 4.2 vs 11.0 ± 3.9 , $p = 0.2$) did not showed statistically difference between groups. Re-bleeding in 3 days occurred in 3 patients (4.2%) in N+CET group and 11 patients (15.7%) in CET only group with statistical significance ($p < 0.001$). Re-bleeding rate in 30 days showed 8.5% (n=6) in the N+CET group while 24.3% (n=17 patients) in CET only groups ($p < 0.001$). There was no reported Nexpowder related adverse events during study period.

Conclusion: Nexpowder application with conventional endoscopic therapy was safe and effective in achieving acute and subacute hemostasis for UGIB. Nexpowder application during conventional endoscopic control might be promising choice for physicians to care in acute emergent UGIB setting.

(Trial registration number: NCT04124588)

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P0042

DIAGNOSIS OF PHARYNGEAL CANCER ON ENDOSCOPIC VIDEO IMAGES BY ARTIFICIAL INTELLIGENCE

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Introduction: A favorable outcome can be expected when pharyngeal cancers are detected at an early stage and they are treated with minimally invasive methods such as endoscopic resection.

Aims & Methods: We therefore aimed to develop an artificial intelligence (AI) system for the real-time diagnosis of pharyngeal cancers.

Methods: Endoscopic video images and still images of pharyngeal cancer treated in our facility were collected. A total of 4559 images of pathologically proven pharyngeal cancer (1243 using white light imaging and 3316 using narrow band imaging/blue laser imaging) from 276 patients were used as a training dataset. The AI system used a convolutional neural network (CNN) model typical of the type used to analyze visual imagery. Supervised learning was used to train the CNN. The AI system was evaluated using an independent validation dataset of 25 video images of pharyngeal cancer and 36 video images of normal pharynx taken at our hospital.

Results: The AI system diagnosed 22/25 (88%) pharyngeal cancers as cancers and 24/36 (67%) non-cancers as non-cancers. The transaction speed of the AI system was 0.03 seconds per image, which meets the required speed for real-time diagnosis. The sensitivity, specificity, and accuracy for the detection of cancer were 88%, 67%, and 75% respectively.

Conclusion: Our single-institution study showed that our AI system for diagnosing cancers of the pharyngeal region had promising performance with high sensitivity and acceptable specificity. Further training and improvement of the system are required with a larger dataset including multiple centers.

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P0043

IN TERTIARY CARE PATIENTS WITH FUNCTIONAL DYSPESIA, POSTINFECTIOUS ONSET IS A RISK FACTOR FOR WEIGHT LOSS

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Introduction: Functional dyspepsia (FD) is a prevalent disease and presents with symptoms located in the epigastric region. The Rome IV criteria differentiate the subgroups postprandial distress syndrome (PDS), mainly characterized by early satiation, postprandial fullness and other postprandial symptoms, and the epigastric pain syndrome (EPS) characterized by epigastric pain or burning. Acute gastroenteritis and H. Pylori infection have been identified as risk factors for FD, in the former case referred to as postinfectious FD (PI-FD). It is unclear how these risk factors relate to Rome IV subgroups and clinical impact. Our aim was to study the association of PI-FD and H. pylori status with clinical profiles, including PDS or EPS, and the amount of weight loss.

Aims & Methods: Consecutive FD patients filled out questionnaires to assess symptom frequency and severity. Patients were identified as PDS, EPS or overlap subgroup according to severity scores of epigastric pain, early satiety or postprandial fullness. Additionally, the postinfectious history and H. Pylori status were determined. Analyses were performed using Chi-square test or ANOVA. Results were considered significant if p< .05. Data are described as mean ± standard error of the mean.

Results: In a cohort of 459 patients with functional dyspepsia (71% females, 39±0.7 ys, 22.2±0.2 kg/m²), 36% were characterized as PDS (n=167, 68% females, 39±1 ys, 21.9.1±0.3 kg/m²), 9% as EPS (n=40, 60% females, 42±2.6ys, 23.3±0.7 kg/m²) and 55% showed overlap (n=252, 75% females, 38±1 ys, 22.2±0.3 kg/m²). Age and BMI were similar in the three subgroups (p=.33 and p=.22 respectively).

Postinfectious onset of symptoms was reported by 20% of patients, 17%, 18% and 23% in the PDS, EPS and overlap subgroups respectively (p=.31). H. Pylori status was positive in 14% of patients, with 12%, 10% and 16% in PDS, EPS and overlap groups respectively (p=.40). Hence, PI onset and active H. Pylori infection were no risk factors for any of the subgroups.

Significant weight loss, defined as more than 5% of the original body weight, was reported by 57% of patients, distributed as 63% in PDS, 36% in EPS and 56% in the overlap group. PI-FD patients were more likely to experience weight loss in the total patient group (OR 2.27, p=.0013) and in the overlap group (OR 3.38, p=.0003) but not in the EPS (OR 2.0, p=.44) or PDS (OR 1.21, p=.70). Only early satiety was associated with significant more weight loss in the PDS (p=.0002) and overlap group (p< .0001).

Conclusion: In this large cohort study, postinfectious onset of symptoms of FD is a risk factor for weight loss, especially in the overlap group, but is not associated with the symptom patterns of PDS, EPS or overlap subgroups.

Disclosure: Nothing to disclose

P0044

FUNCTIONAL DYSPESIA AND ITS SUBGROUPS: PREVALENCE AND IMPACT IN THE ROME IV GLOBAL EPIDEMIOLOGY STUDY

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Introduction: Functional Dyspepsia (FD) is a common Disorder of Gut-Brain Interaction (DGBI), with varying reported population prevalences. The definitions of FD and its subgroups postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS) were updated in the Rome IV consensus.

Aims & Methods: Our aim was to study their prevalences and impact on individuals in an internet survey, as part of the recently completed Rome Foundation Global Epidemiology Study of DGBIs.

54127 adults (26578 females; mean age 43.7, range 18-97 years) in 26 countries completed an Internet survey that included Rome IV FD diagnostic questions, the Patient Health Questionnaire-4 (PHQ-4) psychological distress questionnaire, the PROMIS Global-10 quality of life measure, demographics, and selected medical history. Survey participants were identified and provided by Qualtrics, LLC (Provo, UT). Quota-based sampling was used to ensure a generally comparable sex ratio and age group distributions between countries. Respondents reporting a history of relevant organic disease (peptic ulcer, celiac disease, bowel cancer, or inflammatory bowel disease) were excluded from FD case definition.

Results: Pooled mean Rome IV FD prevalence in the entire sample was 7.2% (95% CI 7.1-7.4). FD rates ranged from 2.2% (Japan) to 12.3% (Egypt). FD prevalence was significantly higher in women, with an odds ratio of 1.56 (1.46, 1.67). FD prevalence decreased with age, from 9.5% in those 18-35 years, to 3.9% in those above 65 (Table). Quality of life physical and mental scores were significantly lower in those fulfilling FD criteria compared to the rest of the population (physical 12.38 (12.30 vs. 12.47) vs. 14.63 (14.61, 14.65)) and mental (11.84 (11.73, 11.95) vs. 13.69 (13.66, 13.72)). The most prominent subtype was PDS, with a distribution of 66.6% PDS, 15.3% EPS and 18.1% overlapping PDS and EPS. Both PDS and EPS were more prevalent in women and decreased with age (Table). Comorbid Rome IV IBS was present in 26.1% of those fulfilling FD criteria,

with lowest prevalence in PDS and highest in the overlap group (13.1% in PDS, 42.2% in EPS, 60.2% in overlap). Functional heartburn and chronic nausea/vomiting criteria were fulfilled in respectively 9.0 and 7.0% of FD cases, with highest prevalence in the overlap group (respectively 26.7 and 18.2%). Fulfilling FD symptom criteria was significantly associated with clinically relevant anxiety (30.4% (28.9, 31.9) to 10.2% (10.0%, 10.5%) and depression (30.2% (28.8, 31.6) vs. 9.9% (9.6, 10.2)) on the PHQ-4.

	Sex	Age group				
		18-34	35-49	50-64	65+	All ages
FD	Females:	10.8 (10.1, 11.4)	8.8 (8.2, 9.5)	7.4 (6.7, 8.1)	5.2 (4.5, 5.9)	8.7 (8.4, 9.1)
	Males:	8.0 (7.4, 8.6)	6.2 (5.7, 6.8)	4.5 (4.0, 5.1)	2.9 (2.5, 3.4)	5.7 (5.5, 6.1)
	Overall:	9.5 (9.1, 9.9)	7.5 (7.1, 7.9)	5.9 (5.5, 6.4)	3.9 (3.5, 4.3)	7.2 (7.0, 7.4)
PDS	Females:	9.3 (8.7, 9.9)	7.5 (6.9, 8.1)	6.3 (5.7, 7.0)	4.5 (3.8, 5.1)	7.5 (7.2, 7.8)
	Males:	6.9 (6.4, 7.5)	5.1 (4.6, 5.5)	3.7 (3.2, 4.2)	2.5 (2.0, 2.9)	4.8 (4.6, 5.1)
	Overall:	8.2 (7.8, 8.6)	6.3 (5.9, 6.6)	4.9 (4.5, 5.3)	3.3 (2.9, 3.7)	6.1 (5.9, 6.3)
EPS	Females:	3.2 (2.8, 3.5)	3.3 (2.9, 3.6)	2.4 (2.0, 2.9)	1.7 (1.2, 2.1)	2.8 (2.6, 3.0)
	Males:	2.4 (2.1, 2.8)	2.6 (2.2, 2.9)	1.7 (1.4, 2.0)	0.8 (0.6, 1.0)	2.0 (1.8, 2.2)
	Overall:	2.8 (2.6, 3.1)	2.9 (2.7, 3.2)	2.0 (1.8, 2.3)	1.2 (0.9, 1.4)	2.4 (2.3, 2.5)

[Prevalence of meeting criteria for Rome IV FD and its subtypes (% and 95% CI) by sex and age groups in the internet sample of adults in 26 countries.]

Conclusion: FD according to Rome IV criteria is highly prevalent on a global scale, affecting more women than men and with declining prevalence with age. FD has a major impact on quality of life and is associated with significant anxiety and depression co-morbidity. PDS is the dominant subgroup, present in over 80% of the FD sufferers. Overlap with IBS, (functional) heartburn and nausea or vomiting is present in only a minority of subjects, and highest in the overlap group.

Disclosure: Nothing to disclose

P0045

THE CORRELATION BETWEEN ELECTRONIC CIGARETTE SMOKING AND DYSPESIA

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Introduction: Dyspepsia is one third case in daily clinical practice and has multiple lifestyle associated risk factors. Tobacco smoking is associated with dyspepsia but the relationship between electronic cigarette (e-cig) smoking and dyspepsia is unknown.

Aims & Methods: This study was aimed to investigate the correlation between e-cig smoking and dyspepsia. This cross-sectional study enrolled 86 adult e-cig smoker in Cirebon City, West Java, Indonesia. We used

consecutive sampling method in this study. The data collection used validated Short-Form Leed Dyspepsia Questionnaire (SFLDQ) in Indonesian language. The dyspepsia was defined as SFLDQ score cutoff ≥ 4 . We also measure the consumption of e-cig smoking, the duration of consumption, and the dose of consumption. Data analysis was using Spearman's rank correlation test.

Results: The prevalence of dyspepsia in this study 38.3%. There is weak correlation between duration of e-cig smoking and dyspepsia ($r = 0.34$; 95%CI: ; $p = 0.03$) but there is no significant correlation between the dose of e-cig smoking and dyspepsia ($r = 0.106$; 95% CI: ; $p = 0.082$).

Conclusion: The dyspepsia in e-cig smoker is prevalent. Further, there is weak correlation between duration of e-cig smoking and dyspepsia. Further studies are needed to determine the correlation between e-cig smoking and dyspepsia and its associated factors.

Disclosure: Nothing to disclose

P0046 WITHDRAWN

P0047

INVESTIGATION OF ESOPHAGEAL EPITHELIAL TISSUE INTEGRITY AND MOLECULAR EPITHELIAL MARKERS ON DIABETIC GERD PATIENTS

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Introduction: Epidemiologically, both Diabetes Mellitus and gastro-esophageal reflux disease are the between most common diseases and have significant impact on public health. The incidence of overlap of these diseases should be high and needs particular attention. We showed that diabetic rabbit EE is more resistant to harmful agents and more powerful LES muscle contractions (1). Therefore it is important to evaluate the pathophysiological mechanisms in the esophageal epithelium (EE) in GERD patients with DM.

Aims & Methods: We evaluated the changes and mechanisms at the EE in two groups of patients (DM+GERD, GERD without DM) and healthy controls. All subjects were underwent 24h pH-MII, esophageal high resolution manometry, upper GI endoscopy and 9 esophageal biopsies in total 57 subjects; healthy controls n=15, GERD n=20, DM+GERD (Type 1 DM n=4, Type 2 DM n=18) n=22. The electrophysiological properties of the esophageal tissues were examined with mini ussing chamber system and the permeability properties were examined with fluorescein spectrophotometrically. E- cadherin and tight junctions mRNA expression levels were determined by quantitative RT-PCR and protein expressions were detected via western-blot and ELISA methods.

Results: : Tissue resistances (R) of DM-GERD have been shown to be significantly higher than GERDs ($p \leq 0.05$), they are also numerically above healthy controls ($p > 0.05$). Diffusion studies revealed that the changes were related with the expansion in the intercellular spaces. When the molecules that play a role in the pathogenesis of DIS were evaluated, the expressions of e-cadherin, ZO-2, Claudin-1, Occludin increased compared to the controls in patients with DM + GERD. Compared to GERD group, ZO-2 and Claudin-1 significantly increased in DM + GERD group. Protein expression results suggest that ZO-2, Claudin-1 increase, and even higher in the presence of DM (Table).

		E- cad	ZO-1	ZO-2	Claudin1	Claudin 4	Occludin
Gene Expression (fold change) *$p \leq 0.05$	GERD / Control	2.08 #	-1.85	1.15	-1.35	1.06	1.09
	DM+ GERD/ GERD	1.45	1.85	1.75 &	-1.12	1.39	-1.02
	DM+ GERD/ Control	3.01*	1.00	2.02*	-1.5	1.47*	1.07
		E- cad (area $\pm$ SD)	ZO-1 (area $\pm$ SD)	ZO-2 (ng/mL $\pm$ SD)	Claudin1 (ng/mL $\pm$ SD)	Claudin 4 (ng/mL $\pm$ SD)	Occludin (area $\pm$ SD)
Protein Expression Level *$p \leq 0.05$	Control (n=15)	0.88 $\pm$ 0.46*	0.71 $\pm$ 0.43	1.2 $\pm$ 0.9 *	1.7 $\pm$ 0.9 *	3.7 $\pm$ 5.4	0.94 $\pm$ 0.58*
	GERD (n=20)	1.17 $\pm$ 1.11	1.07 $\pm$ 0.64	1.7 $\pm$ 2.4 &	2.4 $\pm$ 2.9 &	3.6 $\pm$ 5.3	1.62 $\pm$ 1.51
	DM+ GERD (n=22)	1.68 $\pm$ 1.62*	0.96 $\pm$ 0.87	4.1 $\pm$ 4.1* &	4.3 $\pm$ 2.8 * &	5.0 $\pm$ 4.0	2.01 $\pm$ 1.46*

*Control vs DM+GERD, # Control vs GERD, & GERD vs DM+GERD

[Table]

Conclusion: Presence of DM increased the esophageal epithelial resistance in GERD. This might be related with the changes at upregulation of the molecules especially ZO-2, Claudin 1, Occludin, E-cadherin in the intracellular spaces. It is important for a chronic and years-long disease such as DM to improve molecular properties of EE. These mechanisms of protective changes in the presence of DM in GERD cases also brings the possibility of the target of noxious agents in the epithelium as well as reversing the changes that GERD creates in the esophageal epithelium.

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Disclosure: Nothing to disclose

P0048

DIFFERENTIAL EFFECTS OF DUODENAL BILE SALTS ON MUCOSAL PHYSIOLOGY AND SYMPTOMS IN FUNCTIONAL DYSPEPSIA PATIENTS

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Introduction: Despite increasing evidence for duodenal epithelial hyper-permeability and low-grade inflammation in functional dyspepsia (FD) patients (Vanheel *et al.* Gut 2014), the role of luminal changes has scarcely been studied.

Aims & Methods: We aimed to study duodenal bile salt (BS) concentrations in relation to duodenal mucosal changes and symptoms in FD patients (Rome IV criteria) compared to healthy controls (HC). Duodenal fluids were aspirated via a nasoduodenal tube after endoscopic collection of duodenal biopsies. BS concentrations were measured in fasted state, and in fed state (every 15 min during 1 h; Fortimel®, 300 kCal) using LC-MS/MS. Paracellular passage of a fluorescein-labeled dextran (4 kDa) was recorded in Ussing chambers, and eosinophils were counted on H&E-stained sections per high-power field (HPF; 0.24 mm²). All subjects filled out the Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM). Multilevel (mixed) models were constructed with BS concentrations as dependent and time as independent variables. Univariate and correlation analyses were performed between groups. Finally, mediation analysis was done to study whether mucosal factors (paracellular passage

and eosinophilia) mediated the relationship between BS (total, primary or secondary) and symptoms (PAGI-SYM), with computation of the direct and indirect effect via bootstrapping with 95% confidence interval (CI) using Hayes' PROCESS in SAS.

Results: In total, 24 FD patients (21 female) and 25 HC (16 female) were included with similar age and BMI (Table). A significant effect of time was found for the change in total BS concentrations ($F=23.4$, $p<0.0001$), with a similar evolution for primary and secondary BS in FD patients and HC. Similar total, primary and secondary BS concentrations were found in fed state (45 min) with significantly higher duodenal mucosal permeability, eosinophils and symptoms in FD patients compared to HC (Table). Significant correlations were found between passage and both primary ($r=-0.52$, $p=0.02$) and secondary BS ($r=-0.44$, $p<0.05$) in FD patients but not HC. While only a direct effect of primary BS on PAGI-SYM was seen in FD ($\beta=0.01 \pm 0.004$, $p=0.01$), a significant indirect effect was found of secondary BS on PAGI-SYM, mediated by paracellular passage ($\beta=0.08 \pm 0.05$, 95% CI [0.012;0.19]). When testing the effect of BS on symptoms through duodenal eosinophils in FD, only a direct effect was found for primary BS ($\beta=0.01 \pm 0.004$, $p=0.008$) with no association between eosinophils and secondary BS ($p=0.92$).

Variable, median (IQR)	FD patients (n=24)	Healthy controls (n=25)	FD vs. controls (p-value)
Age (years)	28 (23 - 34)	26 (24 - 32)	0.64
BMI (kg/m ²)	22.3 (19.8 - 23.8)	23.3 (20.1 - 25.7)	0.29
Fed total bile salts (mM)	8.9 (6.1 - 15.6)	8.4 (2.4 - 15.2)	0.39
Fed primary bile salts (mM)	8.1 (5.1 - 12.5)	5.6 (1.7 - 12.5)	0.47
Fed secondary bile salts (mM)	1.1 (0.5 - 2.5)	0.8 (0.2 - 2.3)	0.35
Paracellular passage (pmol)	22.2 (16.1 - 33.0)	19.5 (8.4 - 22.1)	0.02
Duodenal eosinophils (/HPF)	12 (9 - 15)	3 (2 - 4)	<0.0001
PAGI-SYM symptom scores	2.5 (2.0 - 2.9)	0.1 (0.0 - 0.3)	<0.0001

[Between-group comparison of variables of interest]

Conclusion: In FD patients, fed state concentrations of total, primary and secondary BS were similar compared to controls. Fed state primary BS concentrations are associated with symptom severity, independent of duodenal permeability or eosinophils. In contrast, the association of secondary BS with symptoms involved duodenal permeability but not eosinophils. The role of BS in duodenal barrier function, symptom generation, and as a therapeutic target in FD warrant further investigation.

Disclosure: Nothing to disclose

P0049

DEXTRAN SODIUM SULPHATE-INDUCED GASTROINTESTINAL INJURY AFFECTS IMPACT OF DONEPEZIL ON THE GASTRIC MYOELECTRIC ACTIVITY IN EXPERIMENTAL PIGS

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Introduction: Donepezil, a potent reversible cholinesterase inhibitor, has still been used as a preferred treatment of Alzheimer disease. Its gastrointestinal side effects, like dyspepsia, nausea, vomiting or diarrhoea, occur in 20-30 % of patients. Pathogenesis of these motility disorders has not been fully clarified yet. Ageing has a significant impact on the gastrointestinal tract (GIT), even in healthy seniors. Its function can be further deteriorated by an underlying disease. Experimental pigs can be used in pre-clinical studies due to their similar gastrointestinal functions compared with humans. Experimental dextran sodium sulphate (DSS)-induced injury affects function of different parts of the GIT, including the stomach and small bowel.

Aims & Methods: The aim of this study was to assess the effect of a single and repeated doses of donepezil on porcine gastric myoelectric activity with and without DSS-induced injury. Eighteen adult female pigs (mean weight 38.7±1.0 kg) were enrolled. Donepezil hydrochloride was given as a single intragastric dose (group A: 5 mg; group B: 10 mg). The third group (C) received a 7-day donepezil (5 mg per day; in a dietary bolus) with an extra intragastric dose in the morning on day 8 (10 mg). DSS was administered to overnight fasting animals in another dietary bolus in the morning for 7 days (10 g per day). Gastric myoelectric activity was investigated by means of electrogastrigraphy (EGG) on day 1 (A and B) and day 8 (C), using an EGG stand (MMS, Enschede, the Netherlands). All EGGs were performed in propofol general anaesthesia. Basal (15 min.) and study recordings (330 min.) were evaluated by MMS software (version 8.19). Running spectral analysis was used for a standard evaluation of EGG. Results were expressed as dominant frequency of gastric slow waves (DF; cycles per minute - cpm), power analysis (areas of amplitudes; μV^2) and power ratio assessment: fraction of the areas of amplitudes after (numerator) and before (nominator) the study drugs.

Results: Altogether 6210 one-minute EGG recordings were evaluated, each in DF, power and power ratio. Groups A and B revealed similar trends. DF decreased from basal values (median: 3.1; interquartile range: 1.1-3.1; and 3.1; 1.2-3.5 cpm) down in group A (0.9; 0.7-1.2; $p<0.001$) and group B (1.4; 0.9-2.8; $p<0.001$) after 60 min. In group C, DF increased from basal values (2.2; 0.9-3.1) significantly after 105 min. (3.1; 2.8 - 7.0; $p<0.001$). Higher DF sustained for next 165 min. (3.3; 3.3-4.0; $p<0.001$). Power and power ratio had a corresponding pattern.

In group A, power ratio decreased from its highest values 30 min. after drug administration (1.1; 0.4-5.3) to low levels after 120 min. (0.2; 0.1-0.4; $p<0.001$). Group B showed a similar profile. In group C, power ratio dropped significantly from higher values 30 min. from the start (1.0; 0.5-4.7) to low levels after 120 min. (0.4; 0.1-1.1; $p<0.001$). Power ratio raised again after the next 60 min. (1.0; 0.3-6.4; $p<0.001$), finishing with decreased values after 315 min. (0.5; 0.2-0.7; $p<0.001$).

Conclusion: Donepezil alone revealed an unfavourable effect on porcine myoelectric activity assessed by gastric power. It can be a plausible explanation of a donepezil-associated dyspepsia in humans. DSS caused an

undesirable increase in dominant frequency and decreased EGG power. That may indicate that underlying disease in elderly humans can have aggravate the effect of donepezil on gastric myoelectric activity.

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Disclosure: Nothing to disclose

P0050

THE IMPACT OF NABUMETONE ON GASTRIC MYOELECTRIC ACTIVITY IN EXPERIMENTAL PIGS WITH AND WITHOUT GASTROINTESTINAL INJURY INDUCED BY DEXTRAN SODIUM SULFATE

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Introduction: Prostaglandins regulate motility of the stomach. Their inhibition induced by non-steroidal anti-inflammatory drugs may alter gastric motor function. Both, enhanced motility and delayed gastric emptying were described in humans. Nabumetone is a potent, preferentially cyclooxygenase-2 inhibitor. Its non-acidic nature and pro-drug formulation (no entero-hepatic circulation of its active metabolite 6-methoxy-2-naphthylacetic acid) contribute to improved gastrointestinal tolerability of this drug. Experimental dextran sodium sulfate (DSS)-induced injury can have an impact, both, function and morphology of different parts of the gastrointestinal tract, including the stomach and small bowel, and thus affect gastric motor function and intestinal drug absorption.

Aims & Methods: The aim of current study was to investigate the impact of nabumetone on porcine gastric myoelectric activity assessed by a non-invasive surface electrogastrography (EGG) in the setting of presence or absence of injury induced by DSS. Experimental pigs are widely used in preclinical studies owing to their similar gastrointestinal functions compared to humans.

Sixteen experimental adult female pigs (3-month-old; mean weight 38.7 ± 2.3 kg, median 39.0) were divided into three groups treated with nabumetone: A (n=6; a single intragastric (i.g.) dose 1000 mg); B (n=6; a single i.g. dose 2000 mg) and C (n=4; a single i.g. dose 2000 mg after a 7-day DSS administration; 10 g per day, as a morning dietary bolus). All endoscopic intragastric administrations of nabumetone and EGG recordings were carried out in fasting animals under general anaesthesia. Basal (15 min.) and study recordings (eight 15-minute intervals) were accomplished using an EGG stand (MMS, Enschede, the Netherlands). MMS software (version 8.19) was used to assess EGG. Running spectral analysis was used for basic evaluation of EGG. The results were expressed as dominant frequency of slow waves (DF; cycles per minute - cpm). EGG power analysis (areas of amplitudes; μV^2) was accomplished in all animals.

Results: A total of 2160 one-minute EGG recordings were evaluated, each in both parameters. Basal DF of the group C after one-week of DSS administration (mean: 1.9 ± std dev 1.2 cpm) was significantly higher compared with basal DF in groups A (1.5±1.0; p=0.048) and B (1.5±1.2; p=0.013). DF raised in all groups, up to 3.5±3.1 cpm by the end of study recording

(p=0.041; p< 0.001; p< 0.001). For several times, an increase of DF up to 10 cpm, lasting a few minutes, was recorded in different intervals in all groups. Similarly, the basal power of group C was significantly higher (median: 2350; inter-quartile range: 1067-3571; μV^2) compared to groups A (973; 334-2321; p< 0.001) and B (738; 352-3451; p< 0.001). EGG power decreased in all groups by the end of study recording (A: 282; 177-550; p< 0.001; B: 260; 158-968; p< 0.001; C: 757; 391-2581 μV^2 ; p< 0.001).

Conclusion: A single intragastric dose of nabumetone lead to an undesirable increase in dominant frequency and a decrease of EGG power. One-week of DSS administration did not influence the increase of dominant frequency after the administration of nabumetone, but attenuated the fall in EGG power.

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Disclosure: Nothing to disclose

P0051

GASTRIC EMPTYING TIME USING SMARTPILL WIRELESS MOTILITY CAPSULE CORRELATES WITH HUNGER CONTRACTIONS AND HIGH GHRELIN

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Introduction: Many studies quantify gastric emptying with acetaminophen absorption, yielding gastric emptying rate (GER), typically assayed temporally in plasma samples and quantified from time to peak or AUC. For both research and clinical investigations, the SmartPill wireless motility capsule (WMC) is increasingly used to quantify gastric emptying time (GET). Although the two methods are intended to measure essentially the same parameter, physiological variables affecting results can differ. Correlation data between GET and acetaminophen was therefore pursued. In a separate group, correlations between GET, hunger contractions and the metabolic response to a meal in terms of plasma glucose and peptide hormones were studied.

Aims & Methods: WMC recordings with acetaminophen absorption (n=21) and metabolic response (n=41) were obtained from healthy volunteers. Fasted subjects ingested a 260-kcal mixed meal, 1.5g acetaminophen and the WMC. Plasma was obtained -10, 0 (meal intake), 10, 20, 30, 40, 50, 60, 90, 120, 180 and 240 min and stored at -80 °C for later analyses of acetaminophen, glucose, insulin, ghrelin, glucose-dependent insulinotropic peptide (GIP), glucagon-like peptide-1 (GLP-1) and peptide YY (PYY). WMC recordings were analyzed with Motiligi 3.0 software to obtain GET based on pH drop in stomach followed by neutralization upon reaching duodenum. GET was confirmed by last hunger contractions (LHC) by pressure recordings within 5 min before GET. Correlations of GET to LHC, plasma glucose, insulin, ghrelin, GIP, GLP-1 and PYY as evaluated by plasma concentrations as time to peak (Tmax), maximum concentration (Cmax) and exposure (AUC) were quantified by Pearson correlation coefficients.

Results: In all cases, LHC closely reflected GET (R ~0.99). Hence, GET obtained by WMC likely reflected the actual time of WMC migration into the duodenum. By contrast, despite a clear acetaminophen peak 72±4 μM , correlation between GER and Tmax was weak (R ~0.18). Neither did acetaminophen Cmax or AUC correlate with GET. Peptide hormone analyses showed ghrelin to be strongly correlated to LHC (R 0.74; p< 0.0001) and further related to GET (R 0.41, p< 0.02). The timing of GLP-1 meal response

approached significance ($R\ 0.24$, $p < 0.07$), but not C_{max} or AUC. Neither did C_{max} , T_{max} or AUC of glucose, insulin, GIP, or PYY reveal any correlations to GET.

Conclusion: GET as measured by SmartPill WMC displays a robust correlation to hunger contractions occurring at high ghrelin levels, but does not correlate to gastric emptying as measured by acetaminophen absorption, nor to metabolic parameters glucose absorption or insulin release. Hence, hunger contractions seem to be a strong physiological force behind gastric emptying time of the WMC.

Disclosure: Nothing to disclose

P0052

SACCHAROMYCES BOULARDII CNCM I-745 IMPROVES GUT-BRAIN AXIS DYSFUNCTION IN A HUMANIZED MOUSE MODEL OF IBS WITH CO-MORBID ANXIETY

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Introduction: IBS is frequently associated with psychiatric co-morbidities such as anxiety and depression and has been considered a disorder of gut-brain axis communication. We previously developed a humanized mouse model of IBS and co-morbid anxiety (IBS+A) by colonizing germ-free mice with fecal microbiota of IBS+A patients. Bacterial probiotics have been tested in gut-brain axis modulation, but the effects of yeast probiotics such as *Saccharomyces boulardii* CNCM I-745 have not been investigated yet in our humanized mouse model of IBS+A.

Aims & Methods: Our aim was to test the effect of the probiotic yeast *Saccharomyces boulardii* CNCM I-745 (*S. bou*) in preventing gut dysfunction and anxiety-like behavior in our mouse model and investigate underlying mechanisms. Germ-free Swiss-Webster mice were colonized with fecal microbiota from an IBS+A patient or from a healthy subject (HC: healthy controls). Three weeks later, mice were gavaged daily for two weeks with 3g/kg/day of the probiotic *S. bou* (Biocodex-France) or water. Mouse anxiety-like behavior was assessed using the light/dark preference test and the step down test. Mouse gastrointestinal (GI) transit was measured by fluoroscopy after intragastrical gavage with 5 small steel beads and barium sulfate. Barrier function was assessed by Using chamber technique. Gene expression assessed by Nanostring Counter Gene Expression and qRT-PCR. Microbiota was characterized by 16S rDNA and rRNA quantification by Illumina sequencing and qRT-PCR, respectively. Indole quantification was assayed by absorption using Kovak's reagent.

Results: IBS+A mice developed 30% faster gastrointestinal transit ($P < 0.05$) and had a 3-fold longer latency time in the step-down test ($P < 0.001$), indicative of anxiety-like behavior compared with controls. *S. bou* treatment normalized gastrointestinal transit ($P < 0.05$) and shortened by 50% the step-down latency ($P < 0.01$), compared with water-treated mice. Expression of *Trpv1*, implicated in visceral hypersensitivity and anxiety, was 2-fold higher in IBS+A mice than in controls ($P < 0.001$), and its expression was decreased by *S. bou* treatment ($P = 0.05$). Abundance of *Enterococcus*, *Eubacterium*, *Unc. Erysipelotrichaceae*, *Collinsella*, *Butyricicoccus* and *Unc. Coriobacteriaceae* was higher, while *Weissella*, *Fructobacillus* and *Oscillospira* genera were lower in IBS+A mice that were gavaged with water, compared with HC mice. Treatment with *S. bou* normalized those differences. Predicted function analysis suggested higher number of genes implicated in indole biosynthesis in *S. bou*-treated mice ($P = 0.01$). In addition, co-culture of fecal microbiota from SPF mice with *S. bou in vitro* resulted in 20% higher levels of indoles, and 50% higher levels of *Lactobacillus* (which correlated between them - $R^2 = 0.76$, $P < 0.001$).

Conclusion: *Saccharomyces boulardii* CNCM I-745 improves the intestinal and behavioral phenotype induced by IBS+A microbiota in mice. Putative mechanisms include regulation of host *Trpv1* gene expression, modulation of the microbiota and indole production. The results prompt investigation of *S. bou* in IBS patients with co-morbid anxiety.

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P0053

IMPAIRED REGULATION OF AUTONOMIC NERVOUS SYSTEM IN GLOBUS PHARYNGEUS

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Introduction: Globus pharyngeus is one of the more common functional gastrointestinal disorder (FGID). The pathophysiological mechanisms of FGID are complex. However data considering possible cause of globus pharyngeus are scarce. Accumulating evidence indicates that autonomic dysregulation contributes to FGID but whether this is true for globus is still unknown. The symptoms of FGID are often triggered by stress, however, the mechanisms of autonomic dysregulation in FGID, especially in response to stress are incompletely understood.

Aims & Methods: The aim of this study was to assess potential changes of autonomic nervous regulation in patients suffering from globus pharyngeus in response to distinct types of stressors (passive physical stress vs. active mental stress).

Methods: Studied population included 7 patients diagnosed with globus and 10 sex- and age-matched healthy controls. All patients were diagnosed according to ROME IV criteria for functional gastrointestinal disorders. Blood pressure (BP) and heart rate were continuously recorded using Finometer MIDI (FMS, Netherlands) at rest and during two distinct stressors - mental arithmetic test and cold pressor test (cooling of forearm in 1-3°C water bath for 5 min). Evaluated parameters:

- 1) baroreflex sensitivity (BRS, calculated from spontaneous heart rate variability and BP variability) reflex vagally-mediated heart rate regulation in response to changes of BP,
- 2) spectral power in low-frequency band of systolic BP variability (LF-SBP) reflecting sympathetic alpha-adrenergic stimulation of vascular smooth muscles,
- 3) systolic and diastolic BP, and
- 4) mean heart rate.

Results: BRS (reflecting vagal function) in patients with globus was substantially reduced compared to controls at rest and in response to both mental arithmetic test and to cold pressor test ($p < 0.001$ for all comparisons). In contrast, LF-SBP (reflecting sympathetic function) was normal at baseline, but had tendency to be increased in globus group compared to controls during both stress tests. No differences were found in systolic and diastolic BP and heart rate.

Conclusion: Our data show impaired dynamic sympatho-vagal balance in patients with globus pharyngeus at rest and in response to different types of stressors. The vagal function is strongly reduced at baseline and not influenced by stress, while the sympathetic response have tendency to be exaggerated by stress.

These findings support the hypothesis of altered autonomic regulation as a potential mechanism worsening the symptoms of globus with possible contribution of stress as factor. We suggest that comprehensive evaluation

of autonomic response using noninvasive methods could help to better understand the role of autonomic dysregulation in functional gastrointestinal disorders.
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P0054
BRAIN FUNCTIONAL CONNECTIVITY CHANGES IN IRRITABLE BOWEL SYNDROME USING A LACTULOSE PAIN PROVOCATION TEST AND RESTING-STATE FMRI

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Introduction: Irritable bowel syndrome (IBS) is a heterogenous chronic gastrointestinal disorder characterized by chronic abdominal pain associated with altered bowel habits, in the form of diarrhea, obstipation or a mix between the two. The brain-gut axis (BGA) play an important role in IBS, and neuroimaging techniques are useful in the study of brain-gut interactions [1]. Herein, we used resting state functional magnetic resonance imaging (rs-fMRI) to analyse the functional connectivity changes in IBS patients.

Aims & Methods: Eighteen patients with IBS and nine healthy controls (HC) underwent high-resolution anatomical T1-weighted imaging followed by resting state BOLD fMRI scan, twice. After the first scan subjects were administered lactulose (10 mg per os) as a pain provocation test known to induce symptoms in patients with IBS, and the second scan was performed after two and half hours.

Pre-processing of rs-fMRI signals consisted of, removing first two time points, despiking, slice timing correction, co-registration to T1-weighted anatomical images, head motion correction, blurring and nuisance regression. T1-weighted structural MR images were processed using Freesurfer [2] to obtain cortical reconstruction and volumetric segmentation. The T1-weighted MRI segmentations were transformed to fMRI space for extracting the regions of interest (ROIs).

To calculate the functional connectivity (FC) the seed signal was obtained by averaging the pre-processed rs-fMRI time-series from all the voxels in the Freesurfer-segmented insular gyrus region of the left hemisphere. All pre-processing of rs-fMRI signals and the estimation of FC maps were performed using Analysis of Functional NeuroImages software package [3].

Results: Mean of FC values were calculated for the 177 ROIs obtained from Freesurfer segmentation. To identify the ROI with significant changes in FC, two tailed t-tests were performed between mean FC values of IBS patients and healthy controls. Table 1 shows the average FC values over all the IBS patients and HC for some of the brain regions. IBS patients had significantly lower FC values in both the amygdala and the right hippocampus regions. Also, IBS patients have significantly higher FC in right insular cortex compared to healthy controls. Administration of lactulose resulted in significant lower FC values in the amygdala region in healthy controls. However, no significant changes were observed in IBS patients. In the hippocampus regions, FC values of IBS patients were increased, whereas FC values in the same region were reduced in healthy controls.

	Right Amygdala	Left Amygdala	Right Hippocampus	Left Hippocampus	Right Short Insular cortex	Right Thalamus proper
IBS	BL:0.125 AL:0.181	BL:0.134 AL:0.194	BL:0.079 AL:0.170	BL:0.074 AL:0.163	BL:1.075 AL:1.024	BL:0.121 AL:-0.149
HC	BL:0.437 AL:0.193	BL:0.500 AL:0.171	BL:0.315 AL:0.145	BL:0.245 AL:0.142	BL:0.768 AL:0.886	BL:0.083 AL:0.152
p-value (BL)	0.037	0.006	0.023	0.115	0.038	0.748

[Table.1: Mean FC values of IBS patients and healthy controls from both before lactulose (BL) and after lactulose (AL) rs-fMRI scans.]

Conclusion: The IBS patients have significantly different insular cortex resting state functional connectivity maps compared to healthy controls. Also, the administration of lactulose affects the brain differently in IBS patients and healthy controls. In future, comprehensive study of brain activation and connectivity maps using more healthy controls and IBS patients is planned.

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P0055
TRANSCUTANEOUS VAGAL NERVE STIMULATION AS A POTENTIAL TREATMENT FOR FUNCTIONAL GASTROINTESTINAL DISORDERS: A META-ANALYSIS OF NEUROIMAGING EVIDENCE

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Introduction: Autonomic nervous system dysfunction is common in functional gastrointestinal diseases (FGIDs). Attributed to complex underpinning pathophysiology, limited options exist for their medical management. Considering the pivotal role of the vagal nerve in the 'brain-gut axis', transcutaneous vagal nerve stimulation (tVNS) has been proposed as a novel treatment option. However, its precise central mechanism is unknown, which must be concretely ascertained before its widespread uptake in clinical practice.

Aims & Methods: The aim was to identify the reproducible neural correlates of tVNS by meta-analysis. A total of 157 studies were identified from the Web of Science and PubMed databases. 4 neuroimaging studies, encompassing 60 subjects (17 male, 27 female and 16 not provided) aged 18-45, met the inclusion criteria. Using GingerALE meta-analysis of imaging data, activation likelihood estimation (ALE) at the cluster level was calculated. Studies were reviewed for concordance of brain activity in three domains: (1) tVNS vs. baseline; (2) sham stimulation vs. baseline; and (3) tVNS vs. sham stimulation.

Results: tVNS consistently activated regions comprising the insula, thalamus, caudate, medial frontal gyrus and cingulate gyrus and deactivated clusters within the parahippocampal gyri and brainstem (p< 0.0005 Table 1). These findings are consistent with brain regions indicated in vagal nerve activity, interoception and pain processing.

Cluster Ranking	X	Y	Z	ALE score	P-value	Z-score	Location
Brain activation for tVNS vs. baseline							
1	-40	-6	4	0.0111	0.0000	4.2076	Insula (L)
1	-48	44	-16	0.0080	0.0002	3.6020	Middle Frontal Gyrus (L)
1	-42	40	0	0.0077	0.0002	3.4906	Inferior Frontal Gyrus (L)
1	-58	-18	16	0.0074	0.0005	3.2849	Transverse Temporal Gyrus (L)
1	-60	-20	30	0.0074	0.0005	3.2849	Inferior Parietal Lobule (L)
Brain deactivation for tVNS vs. baseline							
1	-30	-46	-8	0.0116	0.0000	4.7882	Parahippocampal Gyrus (L)
1	-6	-28	-24	0.0079	0.0000	3.9969	Brainstem
Brain activation for tVNS vs. sham stimulation							
1	-12	26	44	0.0080	0.0001	3.6600	Cingulate Gyrus (L)
1	-12	38	34	0.0079	0.0001	3.6374	Medial Frontal Gyrus (L)
1	-12	-2	16	0.0074	0.0005	3.3079	Caudate Body (L)
1	-10	-16	10	0.0074	0.0005	3.3079	Thalamus Medial Dorsal Nucleus (L)
Brain deactivation for tVNS vs. sham stimulation							
1	-6	-28	-30	0.0116	0.0000	5.51540	Brainstem

[Table 1: Meta-analytic regions of brain activation and deactivation for tVNS vs. baseline and tVNS vs. sham stimulation in 60 healthy participants]

Conclusion: tVNS reproducibly activates brain areas implicated in the regulatory central autonomic network and deactivates pain processing nodes. Considering the centrality of dysautonomia to FGID pathophysiology, further therapeutic exploration of tVNS is warranted to determine if it can have therapeutic benefit in visceral pain.

Disclosure: Nothing to disclose

P0056

IN PATIENTS WITH HEARTBURN, SUPERFICIAL MUCOSAL AFFERENT NERVES EXPRESS TRANSIENT RECEPTOR POTENTIAL VANILLOID SUBFAMILY MEMBER-1 (TRPV1), AND OESOPHAGEAL EPITHELIAL CELLS EXPRESS ACID-SENSING ION CHANNEL 3 (ASIC3)

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Introduction: Heartburn is a characteristic symptom of gastro-oesophageal reflux disease. This unpleasant symptom is generated at the oesophageal mucosa, where noxious contents of the refluxate interface with nociceptors within the superficial epithelium [1]. We have recently demonstrated superficial afferent nerves in the oesophageal mucosa of patients with non-erosive reflux disease (NERD), but deeper lying nerves in erosive oesophagitis, functional heartburn, and healthy controls [2]. Thus far, these nerves have not been further characterised. Transient receptor potential vanilloid subfamily member-1 (TRPV1) and acid sensing ion channel 3 (ASIC3) are ion channels that can respond to acid and have been implicated in the pathogenesis of GORD [3,4]. TRPV1 mRNA and protein levels are increased in patients with NERD and erosive oesophagitis, and acid-induced activation of ASIC3 sensitises primary oesophageal epi-

thelial cells in culture. The expression of TRPV1 and/or ASIC3 on superficial oesophageal mucosal nerves would strongly support the role of these nerves in heartburn pathogenesis.

Aims & Methods: We aimed to characterise TRPV1 and ASIC3 expression on oesophageal mucosal afferent nerves in patients with heartburn.

We studied 35 patients with heartburn symptoms, and phenotyped them endoscopically and with objective reflux studies into erosive oesophagitis (N=10), NERD (N=10), functional heartburn (N=7), and Barrett's oesophagus (N=8) groups. Mucosal biopsies taken at endoscopy were co-stained with TRPV1 (Alomone, ACC-050, 1:400) or ASIC3 (ThermoFisher Scientific, PA5-61898, 1:200), and CGRP (ThermoFisher Scientific, PA1-30927, 1:400) or E-cadherin (Sigma-Aldrich, 1:100). qPCR was used to assess TRPV1 (Qiagen, QT01010219) and ASIC3 (Qiagen, QT01012557) gene expression in RNA extracted from these mucosal biopsies. Co-localising pixels between TRPV1 and CGRP were quantified with Manders coefficient, and ASIC3-immunoreactive cells were counted using FIJI. Statistical significance among GORD phenotypes was analysed with one-way ANOVA.

Results: In keeping with our previous studies, we found superficial sensory mucosal nerves (within 8 cell layers of the lumen) most commonly in NERD patients (90% of NERD vs 40% in FH). Deep nerves (approx. 22 layers from lumen) were found in 46% of the samples assessed and were most frequently intra-papillary regardless of disease phenotype. Superficial sensory nerves expressed TRPV1 most significantly in NERD (p=0.0057). Deep intrapapillary CGRP positive nerve endings did not express TRPV1 in all phenotypes studied. TRPV1 was occasionally found expressed on epithelial cells. In contrast, ASIC3 was not expressed on nerves, but was expressed on epithelial cells in 43% of samples. ASIC3 was more often expressed in NERD and erosive oesophagitis patients (p=<0.0001).

Conclusion: Superficial oesophageal mucosal nerves, found most frequently in NERD, express TRPV1. Moreover, ASIC3 is expressed predominantly in epithelial cells of NERD and erosive oesophagitis patients. This suggests that superficial mucosal nerves and oesophageal epithelial cells drive acid and pain hypersensitivity. Superficial localisation of TRPV1-immunoreactive nerves and expression of ASIC3 on epithelial cells raise the enticing possibility of topical antagonists as a therapeutic option in treatment of NERD.

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Disclosure: Nothing to disclose

P0057

ASSESSMENT OF THE REFLEX RESPONSE OF THE LOWER ESOPHAGEAL SPHINCTER THROUGH HIGH RESOLUTION MANOMETRY

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Introduction: Hypotonia, increases in abdominal pressure (AP), and transient lower esophageal sphincter relaxations (TLESR) are the main etiological factors of gastroesophageal reflux disease (GERD). The objec-

tive of the study is to assess the possibility of detecting the reflex response of the lower esophageal sphincter (LES) to different stimuli during high-resolution manometry (HRM).

Aims & Methods: A group of patients referred for evaluation of GERD by means of solid state HRM (Medtronic) and 24h pHmetry are studied. Patients with esophageal gastric surgery or major esophageal motor disorders were excluded. 2 groups were defined: Group 1: patients who underwent two abdominal pressure increase maneuvers (manual compression of the abdomen [MCA], and leg elevation [LE]), and Group 2: in which a change in the position from supine position into a sitting position to trigger TLESR.

Results: 73 patients were included: group 1, 35 (19 women) and group 2, 38 (28 women). In group 1, the HRM allowed to identify and quantify the increases in intragastric pressure and the LES reflex response. The mean of the basal gastric pressure was similar in men and women. Gastric pressure increases during LE are much higher than those obtained with MCA (25.7 ± 12 vs. 8.9 ± 3.6). The contractile response was produced mainly by the diaphragmatic component during LE and by the intrinsic LES with MCA. These differences are appreciable only when the 2 components of the gastro-esophageal junction (hiatal hernia) are identified. In group 2, change in position triggered TLESR in 23/38 patients, regardless of the LES resting pressure. The pHmetry showed pathological GER in 14 patients in group 1 and in 19 in group 2. In both the tests were positive more frequently in these patients, although without statistically significant differences, probably due to the small number of cases.

Conclusion: Carrying out these tests during the HRM is easy, does not excessively prolong the study, does not add significant discomfort to the patient, and allows identifying those with an inadequate LES reflex response. The abdominal pressure increases are greater with the LE test, during which the LES response is produced mainly by the diaphragmatic component, unlike what happens during the MCA in which most of the contractile response is carried out by the component intrinsic to the LES.

Disclosure: Nothing to disclose

P0058

PATHOPHYSIOLOGY OF THE INABILITY TO BELCH SYNDROME: OBSERVATIONS MADE WITH PROLONGED ESOPHAGEAL PRESSURE AND IMPEDANCE MONITORING

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Introduction: Symptoms of inability to belch are occasionally reported in gastrointestinal and otorhinolaryngological clinical practices. Although the phenomenon has previously been associated with dysfunction of the cricopharyngeal muscle, its underlying etiology is unclear. Esophageal and pharyngeal air transport patterns and the role of the upper esophageal sphincter (UES) have never been objectively investigated.

Aims & Methods: The aim of this study was to evaluate pathophysiological mechanisms underlying symptoms of inability to belch using prolonged esophageal pressure and impedance monitoring. Consecutive patients presenting with symptoms of inability to belch were included. VAS scores were collected to evaluate esophageal symptoms. All patients underwent

prolonged stationary esophageal high-resolution impedance manometry (HRIM) to assess esophageal motility, UES and lower esophageal sphincter (LES) pressures and relationships with air transport patterns in the pharyngoesophageal region. Patients drank 500 mL of carbonated water to stimulate belching. A subsequent ambulatory pH-impedance study was performed to assess gas reflux patterns and esophageal air presence time over 24 hours. Statistics were presented as medians with range.

Results: We included nine patients, age 25 (18 - 37) years, of whom 5 were male. Gurgling noises from the throat (100%; VAS 8.8 (6.0-10.0)) and bloating (89%; VAS 7.8 (6.4 - 9.1)) were the most frequently reported symptoms. In 8 out of 9 patients, motility was classified as ineffective or absent (distal contractile integral 339.5 (0-753) mmHg $\times$ cm $\times$ s; integrated relaxation pressure 7.2 (3.7-16.2) mmHg). In the majority of patients (89%), UES resting and residual relaxation pressures during wet swallows fell within the normative range (114.0 (71.7-224.9) mmHg and 2.0 (0 - 9.5) mmHg, respectively). After ingestion of the carbonated water, a median number of 42 (14-69) gas reflux episodes up to the level of the lower border of the UES were observed, but none resulted in UES opening. Most events (64%) were followed by a secondary peristaltic contraction. During 24-h pH impedance monitoring, patients reported 10 (5-174) symptom episodes of inability to belch. The majority of these episodes (100% (50-100)) were associated with gas reflux impedance patterns. Moreover, periods of continuous high impedance levels, indicating air entrapment, were observed in all patients. The 24-h esophageal air presence time was 19.9% (2.3-32.6). In all patients, the number of mixed and pure liquid reflux episodes and total acid exposure time were normal (13 (1 - 68) and 1.8% (0.0- 20.2), respectively).

Conclusion: Prolonged HRIM recordings confirm the existence of a syndrome characterized by an inability to belch and support the hypothesis that ineffective UES relaxation, and consequent esophageal air entrapment, may lead to pharyngoesophageal symptoms.

Disclosure: Nothing to disclose

P0059

ACHALASIA IS ASSOCIATED WITH ATOPY IN PATIENTS UNDER 40 YEARS OF AGE

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Introduction: Achalasia is an uncommon motility disorder of the esophagus of unknown aetiology. Associations with autoimmune disorders have been described. Eosinophilic esophagitis (EoE) is associated with atopic conditions such as asthma and eczema. Patients with features of achalasia who are subsequently diagnosed with eosinophilic esophagitis (EoE) and respond to glucocorticosteroids have been previously reported.

Aims & Methods: The aim of this study was to examine associations between achalasia and atopic and autoimmune diseases. A retrospective cohort study using a national primary-care database examined associations between achalasia subjects at both diagnosis and during follow-up, with atopic, autoimmune and neurodegenerative conditions compared with age/sex matched controls. Models were adjusted for age, sex, deprivation, body mass index and smoking status. Due to potential confounding between atopic and autoimmune conditions, subjects with atopic conditions at baseline were excluded when examining associations with autoimmune conditions and vice versa.

Results: Between 1995 and 2018, 2,593 participants with achalasia (median age 57 (IQR 42-72) years; 52% male) were identified, and matched to 10,402 controls. This included 1,082 incident cases, matched to 4,322 controls. At diagnosis, achalasia subjects were at increased risk of autoimmune conditions with 57 (9%) autoimmune conditions in 654 achalasia cases compared to 176 (6%) in 2,866 controls (Odds Ratio 1.39 (1.02-1.90), $p=0.039$). At diagnosis of achalasia, in the whole cohort, there was no association with atopic conditions with 311 (32%) atopic conditions in 964 achalasia subjects compared to 1,133 (28%) in 3,995 controls (OR 1.16 (1.00-1.37), $p=0.53$). However, achalasia subjects under 40 years of age had a 40% increased risk of atopy with 76 (39%) atopic conditions in 195 achalasia cases and 240 (30%) in controls (OR 1.4 (95%CI 1.00-1.95), $p=0.047$). Few incident conditions of interest in achalasia subjects were observed, and no increase in incident rate ratio (IRR) was observed for atopic, autoimmune or neurodegenerative conditions between achalasia subjects and controls. However, an increased IRR was seen for both rheumatoid arthritis and vitiligo individually (2.02 (1.16-3.5), $p=0.012$ and 3.21 (1.07-9.62), $p=0.037$ respectively).

Conclusion: This study suggests that in a subset of younger achalasia patients there is an association with atopy that may have aetiological significance.

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P0060

SYSTEMIC DISEASES ASSOCIATED WITH ABSENT ESOPHAGEAL CONTRACTILITY DISORDER, IT IS NOT ALWAYS SCLERODERMA

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Introduction: Absent contractility is characterized by aperistalsis (100% of swallows with failed peristalsis) and normal median integrated relaxation pressure (IRP). The mechanism and pathogenesis of this disorder is unknown. Absent contractility is associated with systemic autoimmune diseases, especially scleroderma (SSc) and frequently with severe gastroesophageal reflux (GERD), but the evidence is limited on other systemic diseases associated with this esophageal disorder, and only one study has addressed this issue.

Aims & Methods: The aims of this study were to describe the systemic diseases associated with absent contractility and to describe the clinical and manometric characteristics of these patients.

Methods: We performed a retrospective study of all patients diagnosed with absent contractility in our center. We reviewed all high resolution esophageal manometry (HREM) studies performed between May 1st 2018 and February 29th 2020. After careful selection of patients, clinical, demographic, endoscopic and esophageal manometry data were obtained from the electronic medical records.

Results: A total of 1317 HREM were performed in the study period and 72 patients with absent contractility were included for analysis. Overall, 43 (59.7%) were female, with a mean age of 55.4 (+/- 15.0) years. Indications

for HRM were dysphagia in 23 (31.9%) suspicion of GERD in 23 (31.9%), suspicion of autoimmune disease in 18 (25.0%) and miscellaneous in 8 (11.1%).

A comprehensive overview of systemic disorders associated with absent contractility is shown in table 1.

<i>Etiology</i>	<i>cases</i>
Autoimmune disease, n (%)	31 (43.1)
Limited scleroderma, n (%)	14 (19.5)
diffuse scleroderma, n (%)	8 (11.1)
Mixed connective tissue disease, n (%)	6 (8.3)
Sjogren, n (%)	1 (1.4)
LES, n (%)	1 (1.4)
Anti-synthetase syndrome, n (%)	1 (1.4)
Acid-reflux associated, n (%)	25 (34.7)
GERD, n (%)	20 (27.7)
Post-nissen, n (%)	4 (5.6)
Post vagotomy, n (%)	1 (1.4)
Others, n (%)	10 (13.9)
Chronic idiopathic pseudoobstruction, n (%)	3 (4.2)
Steinert myopathy, n (%)	2 (2.7)
CVID / esophageal candidiasis, n (%)	1 (1.4)
Eosinophilic esophagitis, n (%)	1 (1.4)
Chagas disease, n (%)	1 (1.4)
presbyesophagus, n (%)	1 (1.4)
Rumination syndrome, n (%)	1 (1.4)
Unknown, n (%)	6 (8.3)
anti smooth muscle positive, n (%)	1 (1.4)
all test negative	5 (6.9)

[Table 1: systemic disorders associated with absent contractility]

HREM metrics showed a hypotensive LES in 43 (59.7%), with a mean LES resting pressure of 13.9(±11.5) mmHg and a mean integrated relaxation pressure 3.2(±3.4) mmHg, there were no significant differences between groups, interestingly, the presence of a hiatal hernia was more frequent in GERD patients than patients without GERD (36.0% vs 14.9% $p=0.04$).

Conclusion: We found that 34.7% of patients had a different etiology of absent contractility other than GERD or SSc, and even after an extensive evaluation, a definite diagnosis could not be reached in 8.3% of patients.

Disclosure: Nothing to disclose

P0061

BASAL PRESSURE OF LES AND UES: SHOULD WE DETERMINE AT THE BEGINNING OR END OF HIGH RESOLUTION ESOPHAGEAL MANOMETRY?

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Introduction: Manometric parameters of High Resolution Esophageal Manometry (HREM) are defined according to the Chicago Classification (CC). The determination of the basal pressure of the Upper Esophageal Sphincter (UES) and Lower Esophageal Sphincter (LES) is traditionally performed

at the beginning of the HREM in a period of 30 seconds at rest. The invasiveness of intubation and the need to inhibit dry swallowing during determination seems to be the cause of changes in these parameters.

Aims & Methods: To evaluate differences in baseline pressures of the UES and LES when the acquisition of these parameters was made simultaneously at the beginning (standard) and at the end (additional) of HREM. Included patients who underwent HREM with a 36-channel solid state probe (Manoscan®) in supine position, in which an additional assessment of the baseline pressure of UES and LES was carried out at the end of HREM.

Results: Included 76 patients, 60.5% female, with a mean age of 56.6 ± 14.9 years. Most HREM were performed due to GERD (56.6%). In 44.7% of the patients there was a motility disorder according to CC and in 44.7% there was a hiatal hernia. The baseline pressure of the UES (99.6 vs 69.6 mmHg; $p < 0.001$) and LES was statistically different at the beginning and end of the HREM (19.5 vs 17.1 mmHg; $p < 0.001$). At the beginning of the HREM, 40.8% presented hypertensive UES and 3.9% hypotensive, at the end 11.8% hypertensive and 11.8% hypotensive. Regarding the LES, at the beginning of the HREM, 14.5% was hypertensive and 15.8% was hypotensive, at the end, 11.8% was hypertensive and 26.3% was hypotensive.

Conclusion: The baseline pressures of the UES and the LES seem to be statistically higher at the beginning of the HREM when compared to those obtained at the end of the study. These findings may reflect a better patient adaptation throughout the study to the procedure and, probably, the baseline pressure obtained at the end of the procedure maybe more reliable.

Disclosure: Nothing to disclose

P0062

ESOPHAGO-GASTRIC JUNCTION CONTRACTILE INTEGRAL (EGJ-CI) MAY PREDICT RESPONSE TO TREATMENT IN PATIENTS WITH ESOPHAGEAL ACHALASIA

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Introduction: achalasia is defined by the inability of the lower esophageal sphincter to relax in the setting of absent peristalsis. Treatment is focused on reducing symptoms, improve quality of life and prevent complications. Treatments options are actually suggested according to achalasia pattern at high resolution manometry (HRM).

Aims & Methods: The aim of this study was to evaluate the esophago-gastric junction contractile integral (EGJ-CI) and integrated relaxation pressure (IRP) during high and low volume provocative test in a series of patients with achalasia who underwent PD or HDM.

We evaluated consecutive patients with achalasia. All patients underwent upper endoscopy, X-ray and esophageal HRM, Eckardt score. During HRM we evaluated mean EGJ pressure, IRP and EGJ-CI. All patients underwent provocative testing: low volume (multiple rapid swallow, MRS) and high volume 200ml (rapid drinking challenge, RDC) tests. The values of IRP dur-

ing MRS and RDC were collected in all patients. Treatment options were decided according to achalasia HRM pattern, age, anesthesiologic risk and patient choice. All patients were evaluated with X-Ray and Eckardt symptom score 6-month after treatment. According to the treatment efficacy, all patients were divided in: Group A (responder) characterized by no residual dysphagia and normal X-Ray; Group B (non-responder) residual dysphagia and barium retention.

Results: We enrolled 56 patients (27 female) with mean age 60.6 ± 17.8 yrs. All patients had dysphagia and barium retention during X-Ray at baseline. Twenty-eight patients were treated with PD and the same number with HDM. The HRM pattern was: 20 patients with type I, 33 patients type II and 3 type III. According to the patients' outcome, we had 35 patients (18 female) considered as responder and 21 patients (9 female) as non-responder. EGJ-CI were higher in non-responder ($p < 0.001$). During provocative test IRP was lower in responder group ($p < 0.001$). Results detailed in Table 1.

A ROC analysis showed that EGJ-CI (cut-off value 88.95 mmHg-cm) had the best performance (AUC 0.975, sensibility 95.5% and specificity 100%) to predict response to treatment in patients with achalasia undergoing endoscopic or surgical treatment.

	Responder (35)	Non-Responder (21)	p
Male/Female	18/17	12/9	0.934
Mean age (yrs)	59 ± 19.5	60.3 ± 20.2	0.852
EGJ mean (mmHg)	41.4 ± 21.2	56.7 ± 30.4	0.06
Mean IRP-SS (mmHg)	36.5 ± 15.9	43.5 ± 22.7	0.168
EGJ-CI (mmHg-cm/s)	71.9 ± 40.6	120.3 ± 31.1	<0.001
IRP-MRS (mmHg)	31.9 ± 13.7	44.6 ± 14.4	0.0014
Pressurization RDC	13/35	20/21	<0.001
Esophageal dilation (x-Ray)	18/35	10/21	>0.99
Heled-Dor Miotomy	22	8	0.09

[Table 1: data collected during HRM]

Conclusion: Our data suggest that EGJ-CI has the greater diagnostic performance in distinguishing responder to non-responder and should be routinely evaluated in order to choose the best treatment approach for these patients.

Disclosure: Nothing to disclose

P0063

DYSPHAGIA: HAS STANDARDISING OUR TEST MEAL INCREASED OUR DIAGNOSTIC YIELD DURING HIGH RESOLUTION ESOPHAGEAL MANOMETRY?

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Introduction: Non-achalasia major motility disorders (MMD) are part of the diagnostic algorithm of the Chicago Classification for high resolution manometry (HRM) and are notably difficult to manage¹. Further still, few patients presenting with esophageal dysphagia related to MMD report symptoms when swallowing small amounts of water². Inclusion of a standardised solid test meal (rice STM) has been shown to increase the diagnostic sensitivity and specificity for MMD^{2,3}. An alternative approach

used clinically is to ask patients to attend for HRM with foods that usually cause them symptoms; however, it is not known if this provides equivalent results.

Aims & Methods: The primary aim of this diagnostic study was to compare diagnostic yield for MMD of the rice STM with a non-standardised meal, selected by the patient or physiologist. A secondary aim was to compare the likelihood that symptoms were triggered by the test meal.

190 consecutive patients referred for investigation of oesophageal dysphagia underwent oesophageal HRM (24-channel, water-perfused catheter, MUI Scientific, Canada) at the University Hospital of North Durham, UK (Apr 2016-Mar 2020). The presence of symptom-associated major dysmotility during test meals was recorded (symptoms registered within 10s of objective dysmotility). Excluded patients included those with previous MMD diagnosis, previous surgery and failure to complete the HRM study. Half of the cohort received a non-standardised test meal and half were served the rice STM with established reference intervals⁴. Meals required at least 10 swallows to complete. Patients were categorised based on manometric findings (no MMD or MMD). Differences between groups were assessed using the Chi-squared test.

Results: 79 dysphagia patients (42%) met the inclusion criteria for the study. Exclusions were predominantly diagnosis of achalasia (n=50 patients) or diagnosis of a non-achalasia MMD during water swallows (n=36). Of those included, 39 underwent a non-standardised test meal and 40 the rice STM. There was no difference in diagnostic yield or symptom reporting between the two test meals (Table 1). An additional 17 (22%) patients with normal motility or ineffective motility (IEM) during single water swallows had a non-achalasia MMD as a result of solid meal inclusion. Approximately half of these patients, (n=8, six with outflow obstruction), irrespective of test meal had positive "symptom association dysmotility" during the study. A similar number of patients (n=11) had symptoms associated with repeated failed or ineffective oesophageal motility, indicative of clinically relevant IEM⁴.

	Standard test meal (n=40)	Non-standard test meal (n=39)	Significance
Total symptomatic (%)	16 (40%)	13 (33%)	p = 0.54
Total major motility disorder (%)	9 (23%)	8 (21%)	p = 0.83

[Table 1: Manometric findings and symptom associations during test meals.]

Conclusion: The inclusion of a standardised test meal or non-standard testing with solids selected by the patient or physiologist both increased the diagnostic yield of MMD from single water swallow HRM studies by the same extent (overall 22%, in line with prospective case series⁴). The number of patients who reported oesophageal dysphagia during the standardised and non-standard test meals was also similar. These findings confirm that the inclusion of a test meal significantly increases the diagnostic yield of HRM studies; however, as long as sufficient solid swallows are taken (minimum 10), the choice of test meal may not be critical.

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Pharyngeal swallowing and oesophageal motility during a solid meal test: a prospective study in healthy volunteers and patients with major motility disorders. *Lancet Gastroenterol. Hepatol.* 2, 644-653 (2017).

Disclosure: Nothing to disclose

P0064

OVERLAP SYNDROME OF GERD AND DYSPESIA IN THE ORGANIZED URBAN POPULATION OF KHAKASSIA

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Introduction: One of the most actual clinical problems is overlap syndrome of GERD and dyspepsia.

Aims & Methods: In Abakan, a cross sectional study was performed in 1411 people, of whom 905 were alien (Caucasoids, 402 men and 503 women, average age 44.9 years) and 506 indigenous (Khakasses, 276 men and 230 women, average age 41.3 years) inhabitants, which amounted to 93% of the Abakanvagonmash enterprise list. Heartburn was diagnosed in accordance with the Montreal Consensus [1], Barrett's esophagus in accordance with the British Society of Gastroenterology guidelines [2]. Diagnosis of dyspepsia was performed according to the Rome IV criteria [3]. Esophagogastroduodenoscopy was performed in 813 patients in a 50% random sample. Diagnosis of esophagitis was based on the Los Angeles Classification [4].

Results: The prevalence of dyspepsia was 24.3% in Caucasoids and 17.8% in Khakasses (OR=1.48; 95% CI 1.13-1.95; p=0.006). Heartburn was registered in 14.7% of alien inhabitants and in 10.3% of indigenous people (OR=1.50; 95% CI 1.07-2.10; p=0.02); esophagitis - in 3.4% of Caucasoids and 1.9% of Khakasses (OR=1.75; 95% CI 0.70-4.35; p=0.3). The frequency of heartburn was 34.5% in Caucasoids with dyspepsia and 8.3% in Caucasoids without dyspepsia (OR=5.79; 95% CI 3.93-8.52; p< 0.001); 31.1% in Khakasses with dyspepsia and 5.5% in Khakasses without dyspepsia (OR=7.64; CI 4.16-14.02; p< 0.001). Among Caucasoids, esophagitis was recorded in 12.5% of patients with dyspepsia and 0.5% of people without dyspepsia (OR=22.01; 95% CI 5.69-85.17; p< 0.001). In Khakasses, these indicators were, respectively, 8.9% and 0% (OR=55.85; 95% CI 3.04-1025.76; p< 0.001).

Conclusion: The incidence of dyspepsia and GERD was higher among Caucasoids compared with Khakasses. Overlap GERD and dyspepsia were registered in both populations.

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Disclosure: Nothing to disclose

P0065

ESOPHAGEAL MOTILITY PATTERNS AFTER PERORAL ENDOSCOPIC MYOTOMY (POEM) IN PATIENTS WITH ACHALASIA

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Introduction: Several studies have reported partial recovery of peristalsis in patients with achalasia after myotomy.

Aims & Methods: The aim of our study was to analyze esophageal motility patterns after peroral endoscopic myotomy (POEM) and to assess the potential predictors and clinical impact of peristaltic recovery.

We performed a retrospective analysis of prospectively collected data of consecutive patients with achalasia undergoing POEM at a tertiary center. High-resolution manometry (HRM) studies prior to and after POEM were reviewed and the Chicago Classification (CC) was applied.

Results: A total of 237 patients were analyzed. The initial HRM diagnoses were achalasia type I: 42 (17.7%); type II: 173 (73.0%); type III: 22 (9.3%). Before POEM, peristaltic fragments were present in 23 (9.7%) patients. After POEM the CC diagnoses were: 112x absent contractility, 42x type I achalasia, 15x type II, 11x type III, 26x ineffective esophageal motility, 18x esophagogastric junction outflow obstruction, 10x fragmented peristalsis and 3x distal esophageal spasm. Altogether 68 patients (28.7%) had signs of contractile activity, but the contractions newly appeared in 47 patients (47/214, 22.0%). Type II achalasia showed a trend for appearance of contractions ($p=0.097$). Logistic regression analysis did not identify any predictors of peristaltic recovery. The post-POEM Eckardt score was not different between patients with and without contractions nor was the parameters of timed barium esophagogram.

Conclusion: More than 20% of achalasia patients have signs of partial recovery of esophageal peristalsis after POEM. It occurs predominantly in type II achalasia but the clinical relevance seems to be negligible.

Disclosure: Nothing to disclose

P0066 WITHDRAWN

P0067

ENDOSCOPIC CLIPS VERSUS ENDOSCOPIC SUTURE FOR MUCOSAL CLOSURE AFTER PER-ORAL ENDOSCOPIC PYLOROMYOTOMY: A PROSPECTIVE STUDY

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Introduction: G-POEM is an emerging method for treatment of gastroparesis. Safe mucosal closure is necessary to avoid adverse events.

Aims & Methods: The aim of this study was to compare the effectivity of two closure methods: clips and endoscopic suturing (ES) in patients undergoing G-POEM. A single center, prospective study (NCT:03679104). The closure method was assigned at the discretion of an endoscopist prior to the procedure. The main outcome was the proportion of subjects with successful closure. Unsuccessful closure was defined as a need for a rescue method, or a need for an additional intervention. Secondary outcomes were easiness of closure (measured by a visual analogue scale VAS; 0=impossible, 10=very easy, scored by endoscopist and nurse) and closure time.

Results: A total of 29 patients [M:F/13:16, mean age, range: 49.7 (26-74)] have been included; 17 received ES and 12 clips (mean 6; range 4-19). All patients with ES had successful closure. One patient with clips needed a rescue method (KING closure with endoloop) and another two patients needed additional clipping, in one because of a leak on POD1 and another because of periprocedural mucosotomy dehiscence. The remaining 9 patients (75%) had a successful closure with clips. Closure with clips tended to be quicker (mean closure time 10.9 min (range 4-20) vs 14.3 (5-21); $p=0.064$). Endoscopist tended to assess closure with ES easier compared to clips (mean VAS for ES 7.4 (3-10) vs. 6.4 (3-10) for clips; $p=0.18$). A nurse assessed easiness of both closure methods as comparable ($p=0.93$).

Conclusion: Endoscopic suturing system may be more reliable than clipping for mucosal closure in patients undergoing G-POEM. Besides clips, centers performing G-POEM should have an alternative (rescue) closure method. (Supported by a grant from the Czech Ministry of Health 17-28797A).

Disclosure: Nothing to disclose

P0068

POST DEGLUTITIVE UPPER ESOPHAGEAL SPHINCTER MANOMETRIC CHARACTERISTICS ANALYZED WITH SWALLOW-GATEWAY IN PATIENTS WITH ACHALASIA

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Introduction: Abnormal findings of the upper esophageal sphincter (UES) on high resolution manometry (HRM) have been described in patients with achalasia (1,2). In particular, the finding of high UES residual pressure has been postulated to be a protective reflex of the UES to prevent esophago-pharyngeal regurgitation.

Aims & Methods: The aim of our study was to evaluate the post-deglutition UES manometric findings in patients with achalasia to assess the role of UES in preventing esophago-pharyngeal reflux after deglutition.

Methods: retrospective analysis of prospective patients who underwent esophageal HRM in Digestive Physiopathology Unit of ASST Fatebene-fratelli Sacco and San Raffaele Hospital of Milan with diagnosis of achalasia according to Chicago 3 classification; the control group included of patients with diagnosis of normal HRM. HRM analysis was conducted using the Manoview software; UES metric were analyzed using Swallow-Gateway, a dedicated web-based application. Data are reported as means $\pm$ SEM. Student's t test, Mann-Whitney U and chi-square were used as appropriate. P value $\leq$ 0.05 was considered statistically significant.

Results: 18 patients with achalasia and 32 in control group were analyzed. Table 1 reports manometric characteristics of the two groups. Patients with achalasia have higher UES residual pressure and longer UES relaxation; no significant difference was observed for the other parameters evaluated. In particular no difference was observed for baseline and post-deglutitive UES-contractile integral (CI) and UES peak pressure.

	Achalasia	Control	p
UES basal pressure (mmHg)	94.8 $\pm$ 12.7	87.0 $\pm$ 8.2	n.s.
UES residual pressure (mmHg)	9.1 $\pm$ 1.3	3.6 $\pm$ 1.2	0.005
UES time to nadir pressure (msec)	216.3 $\pm$ 26.7	172.6 $\pm$ 16.7	n.s.
UES duration of relaxation (msec)	847.3 $\pm$ 43.3	706.1 $\pm$ 31.5	0.011
UES time of recover (msec)	630.9 $\pm$ 36.4	533.3 $\pm$ 32.7	n.s.
UES-CI baseline (mmHg*sec*cm)	113.7 $\pm$ 22.1	126.6 $\pm$ 24.5	n.s.
UES-IRP median (mmHg)	7.0 $\pm$ 1.0	5.6 $\pm$ 1.1	n.s.
UES-CI post deglutitive (mmHg*sec*cm)	930.0 $\pm$ 98.9	797.2 $\pm$ 38.3	n.s.
UES peak pressure (mmHg)	305.4 $\pm$ 16.2	303.9 $\pm$ 13.6	n.s.

[Table 1. Manometric characteristics of UES]

Conclusion: Our study confirms previous findings of higher UES residual pressure in patients with achalasia compared to control subjects. No difference was observed in the post-swallowing UES characteristics, suggesting that the protective reflex may be present only during the opening of the UES.

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P0069

FUNDOPLICATION IN PATIENTS BORN WITH OESOPHAGEAL ATRESIA: PRE-OPERATIVE WORKUP AND FUNDOPLICATION OUTCOMES

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Introduction: Oesophageal atresia (OA) patients have a higher risk of having a fundoplication compared to other patients with gastro-oesophageal reflux disease (GORD). Fundoplication increases resistance to oesophageal bolus flow, which is already hampered by abnormal oesophageal motility in OA patients. We hypothesized that children born with OA suffer from more post-fundoplication complications including dysphagia compared to non-OA patients.

Recent international guidelines for OA recommend to perform oesophagogastroduodenoscopy (OGD) with biopsies to exclude eosinophilic oesophagitis (EoE), contrast oesophagram to assess upper gastrointestinal anatomy and pH (+/-impedance) measurement to confirm severity of GORD prior to fundoplication (1).

Recent international guidelines for OA recommend to perform oesophagogastroduodenoscopy (OGD) with biopsies to exclude eosinophilic oesophagitis (EoE), contrast oesophagram to assess upper gastrointestinal anatomy and pH (+/-impedance) measurement to confirm severity of GORD prior to fundoplication (1).

Aims & Methods: The aim of this study was twofold. First we evaluated which of these diagnostic tests were performed prior to fundoplication in OA patients in earlier days. Second, we aimed to compare fundoplication outcomes in OA patients with age- and sex-matched peers without OA. Medical records from OA patients and age- and sex-matched controls without OA who underwent fundoplication between 2006-2016 in three international centres (in Australia, The Netherlands and India) were retrospectively reviewed.

Results: 40 OA patients (median 1.1 [0.1 - 17.0]yrs; 88% type C; follow-up 7.9 [0.6-12.0]yrs) and 40 controls (1.3 [0.3 - 17.0]; follow-up 7.5 (0.6-12.0) yrs) were included (table). Preoperative investigations in OA patients included OGD in 34 (85%), contrast oesophagram in 35(88%) and pH(+/-impedance) measurement in 11 (28%). Seven patients 18% underwent all three investigations. Pre-operative OGD (n=34) was abnormal in 12(30%) children, including oesophageal strictures in 6 (18%), EoE in 4 (12%), hiatal hernia in 2(6%), intestinal metaplasia in 2 (5.9%), reflux oesophagitis in 1(3%) and diverticulum in 1(3%).

Post-fundoplication, 33(83%) OA patients had newly developed symptoms including dysphagia(43%), gagging(35%), food aversion(30%), bloating(40%) and/or dumping(8%). No associations between fundoplication outcome and type of fundoplication were found. OA patients had significantly more postoperative dysphagia, bloating and oral aversion compared to controls (table). Recurrent GORD symptoms were seen in 38(95%) OA patients and 13(33%) children developed (recurrent) strictures. In the OA cohort, median time to symptom recurrence was 60 [0-360] days, 95% were back on proton pump inhibitors (PPI) within 2 months post-surgery and 10% had redo-fundoplication.

Conclusion: Our study is the first to examine preoperative diagnostic workup and post-fundoplication outcomes in paediatric OA patients and compare outcomes with a matched control group. Diagnostic workup for

fundoplication in OA patients varies greatly and is often incomplete. Post-operatively, all OA patients had symptoms, including recurrent GORD in 95% who all were back on PPI within two months of surgery. OA patients had significantly more dysphagia, bloating and food aversion post-fundoplication compared to matched controls. The role of fundoplication in OA patients should be re-evaluated. Prospective data is needed to confirm our findings and to develop a tailored treatment paradigm for GORD in OA patients based on symptoms and results of investigations.

Newly developed symptoms	OA patients	Controls	P-value
Dysphagia	17 (42.5)	5 (12.5)	0.005
Gagging	14 (35.0)	9 (22.5)	ns
Dumping	3 (7.5)	1 (2.5)	ns
Food difficulties	12 (30.0)	2 (5.0)	0.006
Bloating	16 (40.0)	7 (17.5)	0.047

[Table. Fundoplication outcome in patients born with OA and age- and sex-matched controls]

References: 1. Krishnan U, Mousa H, Dall'Oglio L, et al. ESPGHAN-NASPGHAN Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Esophageal Atresia-Tracheoesophageal Fistula. *J Pediatr Gastroenterol Nutr* 2016;63(5):550-70.

Disclosure: Nothing to disclose

P0070

ANTRODUODENAL MOTILITY PATTERNS IN PATIENTS WITH GASTROPARESIS: DIFFERENCES BY ETIOLOGY

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Introduction: Gastroparesis (GP) is a common gastrointestinal disorder associated with significant morbidity and considerable health care costs. GP patients form a heterogeneous population with diverse etiology. Treatment is often challenging due to a poorly understood underlying pathophysiology.

Aims & Methods: Therefore, the aim of this study is to assess antroduodenal motility patterns among the different GP etiologies. In this retrospective analysis, we reviewed antroduodenal manometry (ADM) recordings and medical records of patients with confirmed GP between 2009-2019 at Maastricht University Medical Centre. Gastroparesis was diagnosed based on prolonged gastric emptying as measured by scintigraphy or C13 gastric emptying breath test. The following data were collected from medical records: age, gender, BMI, GP etiology and severity grade. ADM was performed using a 36-channel high-resolution manometry catheter. After 30 minutes recording in fasting conditions, patients were given a standardized meal. After the ingestion of the meal, data were recorded for 6 hours, during which patients were not allowed to eat or drink. ADM measurements were evaluated for antral and duodenal amplitudes (mmHg) and motility index (MI), fed period duration (min), number and duration of phase III contractions and migrating motor complexes (MMCs), and presence of neuropathic patterns (i.e. bursts, retrograde propagation, clustered contractions, absence of phase III contractions). Antral hypomotility was defined as antral MI < 13.67.

Results: A total of 167 GP-patients (142 women, median age 45 [31-57]) with confirmed delayed gastric emptying were included. The following GP etiologies were identified: idiopathic n= 101; post-surgery n= 36; diabetes

n= 30. A lower percentage of female patients was found in the post-surgery GP-group compared to the other groups ($p < 0.01$). No differences were found between GP-groups regarding age, BMI, gastric half emptying time, antral and duodenal amplitudes, and MI. Fed period duration was significantly longer in idiopathic ($p < 0.01$) and diabetic GP-patients ($p < 0.05$) compared to post-surgery GP-patients.

Furthermore, the number and duration of phase III contractions, and the number of MMCs was significantly lower in idiopathic and diabetic patients compared to post-surgery GP-patients ($p < 0.01$). Likewise, absence of MMCs during 6-hr recording were more often observed in idiopathic and diabetes GP-patients compared to post-surgery GP-patients (resp. $p < 0.01$ and $p < 0.05$). No significant differences between GP-subgroups were found regarding number of bursts, clustered contractions, retrograde propagation and absence of phase III contractions.

Conclusion: Antroduodenal motility patterns are different between GP etiologies. A disease severity spectrum was identified ranging from post-surgery GP with milder dysmotility patterns to diabetic and idiopathic GP with more severe dysmotility patterns. These differences suggest different pathophysiologic pathways and possible targeted treatment options.

Disclosure: Nothing to disclose

P0071

GASTRIC ELECTRICAL STIMULATION IN PATIENTS WITH TREATMENT REFRACTORY NAUSEA AND VOMITING: A 5 YEAR FOLLOW-UP STUDY

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Introduction: Gastric electrical stimulation (GES) is a treatment option for patients suffering from chronic, refractory nausea and vomiting. It is approved for use in patients with gastroparesis (delayed gastric emptying), but also in patients with normal gastric emptying after positive symptom response during temporary percutaneous GES. The number of patients treated worldwide and studies reporting the long term effects of GES therapy are limited.

Aims & Methods: In this retrospective single-center cohort study, our aim was to investigate the effect of GES over a 5-year period after implantation. All patients implanted with a GES device since 2000 with at least one year of follow-up and at least three self-reported symptom diaries were included.

We have used the same two-week diaries at eight predefined time-points after GES implantation; 1, 3 and 6 months, 1 year and thereafter annually. Symptoms at each time-point were compared with baseline symptoms before GES implantation. A responder to GES treatment was defined by at least 50% reduction in weekly nausea time or weekly vomiting frequency at each time-point.

Overall, patients were considered as complete responders if satisfying the response criteria at $\geq 75\%$ of the time-points, non-responders $\leq 25\%$, and partial responders $> 25\%$ but $< 75\%$. All patients with normal gastric emptying time were selected for treatment after a positive symptom response during temporary percutaneous GES.

Results: Data fulfilling inclusion criteria for symptom reports was available in 68 patients (55 females, median age 43.5 (range 20-81) years), of whom 36 (53%) had five years of follow up. Before GES implantation, the median weekly vomiting frequency was 9.2 (0-177) and weekly nausea time

23 (1-141) h. With our definition of overall long-term treatment response, 42 (62%) patients were classified as complete responders, 21 (31%) patients as partial responders and five (7%) patients as non-responders. The non-responders primarily had idiopathic gastroparesis and were younger ($p=0.045$). There was no difference in gender distribution ($p=0.45$) between the response groups (see table 1). At the last symptom registration time-point, the responder group had reduced their weekly vomiting frequency (median 0 (0-34)) and weekly nausea time (5 (0-133)h) significantly ($p<0.001$ for both), the partial response group showed a trend towards a reduced weekly nausea time (15 (0-49)h) ($p=0.08$), but not for weekly vomiting frequency (7 (0-102)) ($p=0.84$).

The response distribution was similar when comparing patients with delayed vs. normal gastric emptying; complete response 28/46 (61%) vs. 14/23 (61%), partial or non-response 18/46 (39%) vs. 9/23 (39%)

	Responders	Partial responders	Non-responders
Patients (n)	42	21	5
Sex females/males (%females)	36/6 (86)	15/6 (71)	4/1 (80)
Age, years (median, range)	44 (20-68)	44 (24-81)	27 (21-50)
Diagnosis			
Diabetic gastroparesis	16	10	0
Idiopathic gastroparesis	5	2	4
Post-surgical gastroparesis	7	2	0
Enteric dysmotility	7	1	1
Functional vomiting or nausea	7	6	0

[Table 1]

Conclusion: GES has a favorable long-term response in a substantial proportion of patients with chronic severe, refractory nausea and vomiting. However, about one third of patients have partial or incomplete response to treatment with a significant persisting symptom burden. Gastric emptying rate cannot predict the treatment response to GES.

Disclosure: Nothing to disclose

P0072 WITHDRAWN

P0073

STANDARDIZING LONG-TERM GASTROINTESTINAL MOTILITY RECORDINGS IN CHILDREN; COMPARISON BETWEEN HEALTHY ADULTS AND TWO PEDIATRIC POPULATIONS

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Introduction: The most valid method for examining small bowel motility in children is 24-hour antroduodenal manometry. Evaluation of pediatric controls is ethically problematic due to the wearisome procedure of stationary manometry.

Our aim was to evaluate whether 8-hour control recordings from healthy adults can be used as reference for diagnosing pediatric antroduodenal motility disorders.

Aims & Methods: Three groups of subjects underwent antroduodenal manometry; one control group of healthy adult volunteers ($n=43$) and two clinically investigated pediatric groups, one control group with unspecific abdominal pain ($n=15$) and one case group with motility disorders ($n=17$).

Characteristics of phase III and coordinated antroduodenal propagation were compared. Correlation for age was tested for all variables. Ethics approval no. 2020-02496.

Results: The control groups showed recurring MMCs. Children had higher peak pressures of phase III compared to adults (40.1; 36.7-46.9 vs. 31.1; 27.3-44.2 mmHg; $p<0.01$) and shorter duration of phase III (4.8; 4.0-5.7 vs. 6.0; 4.6-7.0 min; $p<0.07$). Frequency and antroduodenal propagation were similar. Within control groups, we found negative age correlation for frequency ($p<0.03$) and positive age correlation for duration of phase III ($p<0.01$). No correlation was found for pressure or antroduodenal propagation.

In the pediatric group with motility disorders, highly irregular motility patterns were discerned with numerically higher peak pressures (43.4; 37.1-55.8) and reduced antroduodenal propagation. PIPO-cases ($n=8$) showed a significantly lower frequency of phase III and prevalent abnormal motility patterns.

Conclusion: The normal phase III in children and adults is not significantly different, except for higher luminal pressures in children. The age correlations within control groups suggest that phase III undergoes changes with growth. We suggest that control values of phase III obtained from healthy individuals can be used across all ages for analysis of antroduodenal motility disorders.

Disclosure: Nothing to disclose

P0074

DEVELOPMENT OF A SCORE THAT PREDICTS MANOMETRIC ALTERATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Introduction: Systemic Scleroses (SSc) comprehends a spectrum of related disorders that share a characteristic of excess of collagen fibers accumulation in tissue. The esophagus is the most frequently affected part of the gastrointestinal (GI) tract. Abnormal esophageal manometry (EM) is present in the majority of patients with SSc. Direct measurement of esophageal motility is usually reserved for patients with symptoms refractory to empiric trial of proton pump therapy. However, approximately 30 percent of patients with EM alterations are asymptomatic.

Aims & Methods: Our aim is to evaluate the relationship between esophageal manometric findings and different clinical and laboratorial findings in patients with SSc and the construction of a model that predicts alterations in EM. We performed a retrospective Cohort study of patients with SSc and EM from a period of 12 years (2008-2020).

We analyzed different clinical characteristics, biochemical, immunologic, electromyographic, echocardiographic and electrocardiographic findings and pulmonary function testing. EM alterations related to SSc were defined as hypotensive lower esophageal sphincter, ineffective motility or absent contractility. Univariable analysis was performed with Man-Whitney for continuous analysis and Qui-square for categorical analysis. We construct a predictive model using backward logistic regression.

Results: We included 71 patients in our study. Eighty-eight were female, median age was 54 (42-64) years. Diffuse cutaneous SSc was present in 10.5%; limited cutaneous SSc in 39.5%; SSc without scleroderma in 1.3% and overlap syndrome with SSc in 42.1%. GI symptoms were present in 82% of the patients (mostly dysphagia, 63%). Upper endoscopy was performed in 75% and endoscopic findings were found in 25% of patients

(erosive esophagitis in 8%, erosive gastritis in 7% and esophageal candidiasis in 3%). EM alterations here present in 40.8% of patients. In univariable analysis, EM alterations relates to Raynaud syndrome (RR 3.6, CI_{95%} 1.3-5.3; p=0.024), diffuse cutaneous SSc (RR 2.5, CI_{95%} 1.5-4.5; p=0.007), anti-nuclear antibody (RR 3.6, CI_{95%} 1.8-4.6, p=0.034), abnormal cardiac study (RR 2.2, CI_{95%} 1.3-4.7, p=0.045) and abnormal CO defuse capacity (RR 1.8, CI_{95%} 1.3-3.2, p=0.021). Abnormal EM was not related to presence of GI symptoms (RR 1.4, CI_{95%} 0.6-3.4, p=0.234). We constructed a model using 4 variables [diffuse cutaneous SSc (1 ponto), anti-nuclear antibody (2 pontos), cardiac study (2 pontos) and CO defuse capacity (4 pontos)], with an area under the curve of 0.748 (p=0.002). Using the cut-off of 5 points, this model presented a sensibility of 86% and a specificity of 74% for detection of EM alterations.

Conclusion: In our population, despite 82% of patients presented with GI symptoms, only 40.8% presented with EM alterations. GI symptoms was not related to EM alterations. Other findings should be considered in order to predict EM alterations. Our model is able to predict EM alterations in patients with SSc. External validation is necessary.

Disclosure: Nothing to disclose

P0075

INEFFECTIVE ESOPHAGEAL MOTILITY: IS SEVERE COMPROMISE RELEVANT?

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Introduction: Ineffective esophageal motility (IEM) is a heterogeneous disorder, considered minor by the Chicago classification, as it is not consistently associated with symptoms. It has recently been proposed to analyze this entity using 3 parameters: severely compromised motility (above 70% ineffective waves), multiple rapid swallows (MRS) and its distal contractile integral (DCI) compared to single swallow (SS), could reveal functional reserve (MRS:SS DCI> 1).

Aims & Methods: Evaluation of these new 3 parameters on IEM patients. Retrospective study of patients with a manometric diagnosis of IEM from 2012 to 2019. We used a high-resolution manometry solid state probe with 36 channels and Sandhill software. Patient with reflux symptoms also performed 24h impedance pH monitoring. Extracted data was further analyzed with SPSS v21.0.

Results: We included 40 patients, 60% (n = 24) female, mean age 56 ± 15 years. The main complaints were heartburn (58%, n = 23) and dysphagia (35%, n = 14), 26 patients underwent pH analysis and 42% (n=11) were positive for pathological gastroesophageal reflux. The MRS:SS DCI ratio was > 1 in 52% of the population.

Severe MEI was identified in 68% of the cases, and was associated with a lower median DCI (255 vs 350 mmHg.s.cm, p = 0.001) but not related to a lower MRSDCI (Severe: 299 vs non-severe: 192 mmHg.s.cm, p = NS), and also not associated with loss of functional reserve (MRS:SS DCI> 1, severe: 70% vs non-severe: 61%, p = NS). Severe MEI was not associated with pathological gastroesophageal reflux (Severe: 35% vs non-severe: 55%, p=NS).

Conclusion: Patients with severe IEM, under this new classification, may still have a preserved functional reserve and were not found to have higher rates of pathological gastroesophageal reflux.

Patients with ineffective motility and reflux could benefit from a complementary study of MRS and their reserve function when being candidates for a potential intervention.

Disclosure: Nothing to disclose

P0076

UPPER ESOPHAGEAL SPHINCTER CHANGES IN ACHALASIA MEASURED WITH PRESSURE-FLOW METRICS

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Introduction: Achalasia is a primary esophageal motility disorder characterized by impaired peristalsis and inadequate relaxation of the lower esophageal sphincter (LES). The main pathophysiological findings are smooth muscle dysfunction in the distal esophagus and lower esophageal sphincter but the whether the disease also affects the upper esophageal function in achalasia is still not clear. Pressure-flow analysis is a new technique which gives a good opportunity to evaluate upper esophageal sphincter (UES) and pharyngeal area by using pressure-flow metrics.

Aims & Methods: The aim of this study was to evaluate UES and area of pharynx by using pharyngeal impedance-pressure manometry in patients with achalasia and to compare with the healthy control group. Achalasia was diagnosed with the measurement of esophageal body and LES with highresolution manometry (HRM), and classified according to Chicago III cassification, timed barium swallow and upper gastrointestinal endoscopy in all patients. High resolution pharyngeal manometry was performed in 27 (16 men; 55,6 ± 15,6 years) naive patients with achalasia and 12 (2 men; 36,5 ± 9,1 years) healthy volunteers.

Different pressure-flow metrics were evaluated. A solid state catheter with 36 pressures and 16 impedance channels was used and calibrated with Software Version 9.4 Medical Measurement Systems (MMS) database. Procedures were performed in semi-sitting position with receiving 3 times 5 ml and 3 times 10 ml isotonic liquid swallows. After the UES and pharynx values were recorded, the procedure was terminated and the catheter was removed. The manometry tracings were uploaded to Swallow Gateway system. This webpage and incorated software spesifically design for the evaulation of mesurements a combined impedance mea- surements.

Results: Upper esophageal sphincter relaxation pressure (U-IRP), hypo-pharyngeal intrabolus pressure (H-IBP) and pharyngeal pressures (PHCI) significantly higher in patients with Achalasia compared to HC. There were no significant differences between two groups in terms of UES Maximum-Admittance (Max. Adt.) and Bolus Presence Time (BPT) metrics (Table).

		Patient Group (mean±SD)	Healty Control (mean±SD)
5 ml	Max. Adt. (mmHg)	2,94±0,84	4,59±0,75
5 ml	H-IBP (mmHG)	10,12±10,72*	3,32±6,30
5 ml	U-IRP (mmHg)	8,58±10,91*	-1,42±8,12
5 ml	BPT (sn)	0,57±0,11	0,57±0,07
5 ml	PHCI (mmHg*s*cm)	497,70±210,00*	334,58±120,71
10 ml	Max. Adt. (mmHg)	5,81±0,01	5,56±0,56
10 ml	H-IBP (mmHG)	10,11±10,92*	3,15±7,01
10 ml	U-IRP (mmHg)	10,81±10,08*	-,17±7,76
10 ml	BPT (sn)	0,64±0,23	0,61±0,12
10 ml	PHCI (mmHg*s*cm)	516,43±222,8*	331,79±109,50

*p< 0.05 compared to controls

[Table]

Conclusion: UES relaxation was significantly insufficient in patients with achalasia compared to HC. We speculate that in order to facilitate the passage of UES bolus against the difficulty of relaxation, pharyngeal pressures and intrabolar pressure increased. The insufficiency at UES relaxation might be explained with two possibilities; 1) There might be similar but lesser degree pathology within UES nerves and muscles to constraint against a sufficient relaxation 2) Because of the accumulation of food and secretions inside the esophagus, intraesophageal pressure increases in Achalasia patients and this facilitates the aspiration of the content. Increased U-IRP might be reflection of protection of upper airways. Further studies comparing UES pressure flow metrics before and after successful management might be helpful.

Disclosure: Nothing to disclose

P0077

THE EFFECT OF PROTON PUMP INHIBITOR PLUS ALGINATE THERAPY ON HIGH-RESOLUTION MANOMETRY PARAMETERS IN GASTROESOPHAGEAL REFLUX PATIENTS WITH INEFFECTIVE ESOPHAGEAL MOTILITY

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Introduction: The ineffective esophageal motility (IEM) in according to the Chicago classification is that the distal contractile integral (DCI) is below 450 mmHg.s.cm. in more than half of wet swallows. IEM detected on high-resolution manometry (HRM) is the most common esophageal motility disorder in gastroesophageal reflux patients. However, the direction of association between reflux disease and IEM is unclear.

Aims & Methods: We aimed to show the effect of PPI (twice a day) plus alginate (four times a day) therapy on esophageal motility in gastroesophageal reflux patients with IEM in our study.

The effects of six months PPI plus Alginate therapy on HRM parameters in gastroesophageal reflux patients with IEM were retrospectively analyzed.

Results: Sixteen gastroesophageal reflux patients with IEM who underwent post-treatment HRM were found. Eight of patients (50%) were female, the mean age was 48±14.4 years. IEM was not detected in 11 of 16 patients (69%) in post-treatment HRM analysis. The weak peristaltic contraction percentage decreased in three of the remaining five patients and in two patients did not change. The mean DCI was found to be significantly higher in the post-treatment HRM than pretreatment procedure (609.1 ±317.1 vs 349.9 ± 200.9 mmHg.s.cm. respectively, p=0.01). In the HRM examination performed after the treatment, the percentage of normal peristaltism in wet swallows was statistically significantly higher than the percentage of normal peristaltism before treatment (75±15.9 vs 45.6±30.8, respectively. p=0.002).

Conclusion: In reflux patients with IEM six months PPI (twice a day) plus alginate (four times a day) therapy increases the mean DCI in the esophageal body and improves IEM in 69% of patients.

Disclosure: Nothing to disclose

P0078

THE RELATION BETWEEN CHANGES IN GASTRIC EMPTYING RATE AND IMPROVEMENT OF SIMULTANEOUSLY MEASURED SYMPTOMS WITH PROKINETIC AGENTS; AN ANALYSIS OF 8 TREATMENT TRIALS

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Introduction: Meta-regression analyses have failed to show a significant relationship between improvement of gastric emptying rate (GE) and improvement of symptoms with prokinetic agents in idiopathic gastroparesis (IGP)/functional dyspepsia (FD). However, significant effects emerge when a selection of agents and tests is applied (Janssen 2013; Vijayvargiya 2019). The potentially strongest link between effects on GE and symptoms is found when both are measured simultaneously. We studied this relationship at the individual patient level in treatment intervention studies performed by our unit.

Aims & Methods: Data from 6 placebo-controlled cross-over trials and 2 open label studies involving ghrelin, prucalopride, cisapride, botulinum toxin (BT), buspirone, erythromycin, clonidine and octreotide; (2 acute, 6 repeat administration) in 140 FD/IGP patients, were analysed. All patients underwent a standardized GE breath test (13C-octanoic acid) during which the intensity (0-4) of fullness, bloating, nausea, belching, epigastric pain and burning (EB) were scored every 15 min for 4 hours. Meal-related severity of individual symptoms (ISS) was obtained by summing all scores for that symptom and the overall meal-related symptom severity (OSS) was defined as the sum of all individual symptoms scores. The relationship between change in GE T1/2 and change in symptom score was assessed via Spearman correlation in individual and pooled studies.

Results: Overall, GE improved during treatment (p< 0.001), OSS (88±7 to 63±6, p< 0.0001) and all ISS except EB were improved (all p< 0.005). OSS as well as ISS did not correlate significantly with GE T1/2, at baseline/placebo or during active treatment (respectively R=0.01 and R=-0.03). The change in GE T1/2 did not correlate with the change in OSS (Fig.1) or the change in ISS (all R-values < 0.12). Individual studies with BT, erythromycin and prucalopride showed significant improvement in GE T1/2, but no significant positive correlation was found for the studies separately (respectively R=-0.42, -0.28 and 0.23) or pooled together (R=-0.13).

Conclusion: Even in the closest apposition between measurement of GE and symptom assessment in FD/IGP, no correlation was found between the degree of symptom improvement and the improvement of GE. The observed symptomatic significant benefit must be attributed to effects other than enhanced GE.

Disclosure: Nothing to disclose

P0079

ENDOSCOPIC NOVEL COMBO TECHNIQUE: LONG-TERM OUTCOMES IN TREATING PATIENTS WITH PRIMARY ACHALASIA

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Introduction: Achalasia is a primary esophageal motility disorder characterized by the absence of esophageal peristalsis and impaired relaxation of the lower esophageal sphincter (LES) in response to swallowing.

Aims & Methods: Evaluating combined Botulinum toxin injection, pneumatic dilation and mechanical dilation by retro-flexion of the endoscope (COMBO) as a suggested novel treatment for achalasia.

Methods: The study included 44 Egyptian patients suffering from achalasia of the cardia (AC). The suggested COMBO technique is done in single step endoscopic setting three-steps procedure:

1- Injection of 100 Units Botulinum toxin type A (Botox-Allergan), 25 units circumferentially in anterior, posterior and lateral esophageal wall.
2- Wait about 1-2min and pass the scope to the stomach and then graded dilatation using Achalasia balloon over guide wire starting from 35 mm to be followed 3 min later by 40 mm balloon dilation, time of inflation should not less than 1 min.

3- Inspecting the cardia carefully after balloon dilatation then retroflexion of the scope and inspecting the cardia and rinse it thoroughly with water then approaching the cardia carefully with the scope retro-flexed with right axis deviation by using the right-left knob of the scope and trying to gently insinuate the scope to the esophagus through the cardia but only 2/3 of the retroflexed portion (the maximum circumference of the semi-circular part) of the scope and not the entire endoscopic shaft so the semi-circular portion of the retroflexed part is kept dilating the cardia for about 30 seconds with rotating the scope in a gentle way 180 °C gently during this period using hand and body rotation to rotate the scope and repeat it at least three time. (The action is not allowed if there is a difficulty insinuating the retroflexed scope through the cardia).

Finally good endoscopic inspection of the dilated lower esophageal sphincter must be done for detecting any complications mainly bleeding or perforation, so we recommended better rinsing with methylene blue to exclude any area of perforation that was done for all cases after dilatation.

Results: The Combo endoscopic method showed a very good and satisfactory response in 42/44 of patients (response rate 95.5%) from the first session with a follow up period ranging from at least 48 weeks to maximum of 240 weeks.

All Patients showed significant improvement of almost all the clinical symptoms especially dysphagia, regurgitation, choking and postprandial vomiting even the patient who experienced iatrogenic post Heller myotomy (follow up 50 weeks), 8/44 (18.1%) patients still experienced infrequent non-annoying retrosternal chest pain, 12/44 (27.2%) suffered intermittent heart burn and mild regurge.

No complications were reported during or after the procedure as perforation or bleeding.

Conclusion: COMBO endoscopic technique could be suggested as a novel and effective method for treating achalasia as a stepwise way before proceeding to more risky invasive methods as Peroral Esophageal Myotomy (POEM) or surgical procedure or in high risky patients at least.

Disclosure: Conflict of interest and funding: Non

P0080 WITHDRAWN

P0081

ENDOSCOPIC FINDINGS AT THE TIME OF FOREIGN BODY IMPACTION REMOVAL: A 7 YEAR RETROSPECTIVE AUDIT

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Introduction: Foreign body impaction (FBI) is a frequent gastroenterological emergency. The management of FBI usually requiring urgent endoscopy to retrieve the obstruction, but is also useful in the potential diagnosis of the underlying cause for FBI. Currently, limited studies detail an underlying cause for FBI at initial endoscopy for removal of the obstruction.

Aims & Methods: This study aimed to assess the endoscopic diagnosis of the underlying cause for FBI at initial endoscopy. Details of all patients who presented with FBI to Central Coast Local Health District (Gosford Hospital and Wyong Hospital) from 2013 to 2020 were reviewed from a retrospective database. Detailed admission and endoscopic findings were examined for patients admitted under the Gastroenterology team.

Results: From January 2013 to January 2020, 311 patients presented with food bolus impaction to Gosford or Wyong hospitals during the audit period. The majority of these patients were male, at 76.3%. The average age at presentation was 56.5, and the age of presentation trended towards younger age groups however, this was non-significant. Of those patients presenting with FBI, 277 (89%) underwent endoscopy, with 34 (11%) patients spontaneously clearing their impaction. On endoscopy, 234 (75%) patients had food product present in their oesophagus requiring removal. 37 (15%) patients had a diagnosis for the underlying cause of their food bolus obstruction made. These were eosinophilic oesophagitis (17), reflux stricture (5), ill-defined stenosis (3), hiatus hernia (3), pill oesophagitis (3), tortuous oesophagus (2), Zenkers diverticulum (1), pharyngeal pouch (1), Schatzki ring (1), and carcinoma (1). 197 patients had no cause identified for FBI on initial endoscopy.

Conclusion: 75% of patients presenting with FBI had food product present on initial endoscopy. Only 15% of patients who presented with food bolus obstruction had a clear diagnosis for the underlying cause identified on initial endoscopy. This study reaffirms the need for further endoscopic investigation following FBI to identify an underlying diagnosis for the obstruction.

Disclosure: Nothing to disclose

P0082

CLINICAL SPECTRUM AND TREATMENT OUTCOMES OF EOSINOPHILIC OESOPHAGITIS IN DURHAM AND TEES VALLEY, INCLUDING INITIAL RESULTS OF ORODISPERSIBLE BUDESONIDE (JORVEZA®)

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Introduction: Eosinophilic oesophagitis (EoE) is common in pts with dysphagia or food bolus obstruction. Swallowed steroids have been the mainstay of treatment until Orodispersible tablet (ODT) Budesonide (Jorveza®) became available in 2018. The real world outcomes of ODT budesonide are awaited.

Aims & Methods: This retrospective study, designed after the launch of ODT budesonide in the UK, aimed to (1) analyse the current clinical presentation, (2) endoscopic diagnosis, and (3) treatment outcomes with proton pump inhibitors (PPI), swallowed steroids (Fluticasone or Budesonide inhalers) and ODT Budesonide (Jorveza®).

Patients with histologically confirmed EoE (defined by a eosinophil count of >15/hpf) between Jan 2018 - Jun 2019, were identified from a histology database at 2 large University hospitals. Clinical presentation, endoscopy findings, treatments and outcomes were extracted from electronic patient records. Patients with eosinophil counts of 5-15/hpf were included as "possible EoE". Symptom improvement was defined as >50% reduction in dysphagia episodes weekly.

Results: 59 pts (38M, 21F) with confirmed or possible EoE were identified. 44% were between ages 40-60yrs. 64% were male. 54% had history of atopy - asthma and hayfever being common. 10% pts reported food allergy. 71% pts were non-smokers. Dysphagia was the presenting symptom in 84%, predominantly to solids (76%). 40% reported having some form of food bolus obstruction. Other symptoms included heartburn (47%), regurgitation (40%), and vomiting (31%). Endoscopy EREFS Scores were: 0=18, 1=26, 2=12, 3=3. Biopsy (Bx) distribution was 1-2 Bx =17pts, 3-4 Bx =30, 5-6 Bx = 12. No strictures requiring dilatation were present. 40/59 patients had been trialed on a PPI with only 32.5% improvement. 21/59 pts were treated with swallowed corticosteroids, 18 pts had >6month follow up, with 56% symptom resolution. 20 pts were treated with ODT budesonide for 12 weeks, 6 after non-response to swallowed steroids. Overall symptom resolution in this group was 50% (9/18). 100% response in treatment naïve pts, and 67% response in those who had previously received swallowed steroids. Response rates between Jorveza treated and swallowed steroid pts was not statistically significant, due to small sample sizes, p=0.74.

Conclusion: Eosinophilic oesophagitis is still being diagnosed at a later age of between 40-60yrs. There is significant variability in the number of oesophageal biopsies taken at endoscopy. The initial results of ODT Budesonide treatment are promising, especially in treatment naïve patients.

Disclosure: Nothing to disclose

P0083

RELATIONSHIP BETWEEN SYMPTOMS AND CLINICAL FEATURES IN PATIENTS WITH ESOPHAGEAL EOSINOPHILIA

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Introduction: There are patients with eosinophilic esophagitis (EoE) who have symptoms such as chest pain or dysphagia, while there are asymptomatic patients with esophageal eosinophilia. It is known that EoE patients are likely to have esophageal motility abnormalities that may cause their symptoms. However, a relationship between symptoms and clinical features in patients with EoE are not known.

Aims & Methods: The aim of the study was to reveal the association between symptoms and clinical features in patients with esophageal eosinophilia.

A total of 20 patients with esophageal eosinophilia (eosinophil infiltrations in the esophageal mucosa ≥ 15 /HPF) who underwent both esophagogastroduodenoscopy (EGD) and esophageal high-resolution manometry (HRM) were enrolled between 2009 and 2018. Dysphagia, chest pain, and heartburn were classified as typical symptoms and nausea, abdominal pain, bloating were classified as atypical symptoms. Characteristic EGD findings (circular rings, linear furrowing, white exudates), HRM findings evaluated by Chicago classification, and treatments were assessed by each patient's symptom.

Results: Dysphagia (9 cases, 45%), chest pain (7 cases, 35%), heartburn (5 cases, 25%), and atypical symptoms (5 cases, 25%) were observed. HRM revealed abnormal esophageal motility (11 cases, 55%): esophagogastric junction outflow obstruction (EGJOO) (3 cases, 15%), Jackhammer esophagus (2 cases, 10%), distal esophageal spasm (1 case, 5%), ineffective esophageal motility (IEM) (5 cases, 25%), and normal (9 cases, 45%). Patients with dysphagia had significantly higher integrated relaxation pressure (IRP) (12.9mmHg) and higher distal contractile integral (DCI) (3789.6mmHg-cm-s) than patients without dysphagia (9.1mmHg, 1069mmHg-cm-s, $P < 0.05$ each). Patients with only atypical symptoms had lower IRP (7.46mmHg vs. 11.95mmHg, $P < 0.05$). Dysphagia was related to EGJOO and spastic disorders than IEM and normal. The type of symptom was not associated with any endoscopic finding nor eosinophil counts in esophageal epithelium. Regarding the treatments, 2 patients did not take any medication, 13 patients only had proton pump inhibitor (PPI) therapy, and 5 patients needed steroid after PPI trial. Patients with chest pain tended to be treated with steroid ($P < 0.05$).

	Dysphagia		Chest pain		Heartburn		Atypical symptom	
	+	-	+	-	+	-	+	-
No of patients	9	11	7	13	5	15	5	15
Age, y	48.1 ±6.7	46.7 ±12.2	49.0 ±8.7	46.5 ±10.7	50.4 ±4.9	46.3 ±10.8	42.8 ±16.7	47.8 ±6.6
Sex (M:F)	6:3	9:2	4:3	11:2	4:1	11:4	4:1	11:4
Endoscopic finding +	6(67%)	7(64%)	4(57%)	9(69%)	4(80%)	9(60%)	3(60%)	10(67%)
HRM parameters: IRP (mmHg)	12.9 ±3.1	9.1 ±2.9*	11.9±3.4	10.3±3.6	12.9±3.5	10.1±3.3	7.46±2.8	12.0±3.0*
DCI (mmHg-cm-s)	3789.6 ±4724.2	1069.0 ±904.3*	3429.1 ±5520.0	1681.7 ±1490.2	1901.4 ±1411.1	2423.9 ±3913.1	1259.0 ±1356.0	2638.1 ±3862.6
EGJOO/spastic/IEM/normal	2/3/0/4	1/0/5/5*	2/1/2/2	1/2/3/7	2/1/1/1	1/2/4/8	0/1/2/2	3/2/3/7
Treatment: PPI/steroid after PPI trial	6/3	7/2	2/4	11/1*	3/2	10/3	4/1	9/4

[Characteristics of clinical data in each symptom in patients with esophageal eosinophilia *: $p < 0.05$]

Conclusion: Esophageal motility abnormalities with higher IRP and DCI are suggested to be related to dysphagia. PPI therapy might be ineffective to relieve chest pain and patients with chest pain tended to need steroid therapy in patients with esophageal eosinophilia.

Disclosure: Nothing to disclose

P0084

LIPID PROFILING IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is the second most common inflammatory disease in the esophagus [1]. EoE is an antigen-driven immune-mediated reaction clinically characterized by symptoms of esophageal dysfunction and histologically defined by an eosinophil-predominant inflammation in the esophagus [2]. Long lasting eosinophilic inflammation leads to fibrosis with stricture formation as presented by dysphagia and bolus obstruction [3, 4]. Until now mechanisms of inflammation in EoE are not fully understood. Some findings indicate a role for lipid mediators in these inflammatory processes.

For instance, it has been shown that 15-lipoxygenase (LOX), a key-enzyme in the arachidonic acid cascade, is up-regulated in esophageal tissue in active EoE. Additionally, PGD₂ receptor antagonists [5] may serve as therapeutic options besides topicals steroids and elemental diet.

Aims & Methods: We have recently shown that comprehensive lipid mediator profiling is feasible in gastrointestinal (GI) tract tissue biopsies [6]. Therefore, we now aim to get deeper insights into lipid mediator modification occurring in EoE.

Oxylipine patterns in esophageal tissue of 13 patients with active EoE compared to healthy tissue of 15 patients without EoE were analyzed. Lipid metabolite profiles were determined by liquid chromatography coupled with tandem mass spectrometry.

Results: We detected significantly elevated levels of cyclooxygenase-(COX) derived prostanoids of the D and E series in active EoE. Furthermore, we found significantly increased levels of 15-HETE, 15-HETe, 17-HDHA and other hydroxy-PUFA which can be formed by 15-LOX and COX, in active EoE esophageal tissue compared to controls.

Conclusion: Our findings support the hypothesis that COX- and 15-LOX-derived lipid mediators are part of the inflammatory processes occurring in EoE. These findings warrant further research to investigate their role as potential therapeutic targets.

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Disclosure: Nothing to disclose

P0085

PROVOCATIVE TESTS DURING HIGH-RESOLUTION MANOMETRY MAY BE HELPFUL TO DISTINGUISH PATIENTS WITH EOSINOPHILIC ESOPHAGITIS RESPONDING TO PPI THERAPY

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Introduction: Eosinophilic esophagitis (EoE) is an up-and-coming condition histologically characterized by 15 eosinophil x HPF from esophageal biopsies. Proton pump inhibitor (PPI) represents the first line approach of this condition. No demographic or clinical parameters have found able to predict response to treatment. Standard high-resolution manometry (HRM) did not show any specific motor findings in patients with EoE.

Aims & Methods: The aim of this study was to evaluate the role of low (multiple rapid swallow, MRS) and high volume (rapid drinking challenge, RDC) provocative tests in predicting histologic remission after PPI therapy in patients with EoE

We evaluated consecutive patients with EoE who underwent HRM and reflux monitoring (impedance-pH) to exclude GERD. HRM was performed according to Italian guidelines. All patients had 3 MRS (5 wet swallows of 2ml of water in less than 10s) and one RDC (200ml of water swallowed rapidly).

Thereafter, the same treatment with high dose PPI (80mg esomeprazole for 8 weeks) was administered to every patient, which was followed by a routine endoscopy with 6 esophageal biopsies. According to histology patients were categorized in: responder (< 15 Eos x HPF; Group A) and non-responder (>15 Eos x HPF). The results of HRM and MII-pH were evaluated to better understand differences between the two groups.

Results: We evaluated 29 patients (6 females; mean age 29.7±11.7 years; mean BMI 21.5±1.2). Group A was composed by 14 patients (4 females; with mean age of 26.6±10.3); Group B was composed by 15 patients (2 females; with mean age of 32.4±13.4) (p< 0.05). GERD was excluded in all patients and impedance-pH did not show any significant differences between the two groups. HRM did not show any difference between the two groups in terms of esophagogastric junction parameters and esophageal body motility during the 10 wet swallows. However, MRS and RDC showed a lack of inhibition of esophageal body with frequent panesophageal pressurization (p< 0.001). Data from HRM were summarized in Table 1.

Conclusion: Provocative tests during standard HRM seem able to distinguish responder from non-responder to PPI treatment. These preliminary results, if confirmed by larger and prospective studies, will be useful to choose steroids or diet as first-line approach for treating EoE patients.

Disclosure: Nothing to disclose

	Group A (14pts)	Group B (15 pts)	p
Mean DCI-SS	2482.7±911.4	1915.1±589.4	0.052
Mean IRP-SS	10.6±2.6	13.6±4.1	0.131
Mean DCI-MRS	2408.5±1014.6	1802.1±992.7	0.173
Mean IRP-MRS	10.5±3.3	13.1±3.2	0.067
Failed MRS	2	9	0.02
Pan-esophageal pressurization-MRS	1	10	0.001
DCI-RDC	705.8±214.9	684.3±116.8	0.768
IRP-RDC	11.6±2.6	14.3±4.1	0.076
Failed RDC	5	13	0.007
Pan-esophageal pressurization-RDC	1	11	<0.001

[Table 1: data collected during HRM]

P0086

FIBROTIC FEATURES IN THE EOSINOPHILIC ESOPHAGITIS ENDOSCOPIC REFERENCE SCORE IN THE DIAGNOSIS AND RESPONSE TO PROTON-PUMP INHIBITOR THERAPY

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Introduction: The eosinophilic esophagitis (EoE) Endoscopic Reference Score classification system is proposed to standardize the reporting of major endoscopic features of EoE, which are included in the acronym EREFS. The validated EREFS system may help to identify inflammatory (edema, exudates and furrows) versus fibrotic features (rings and strictures) in the esophagus of EoE patients. Proton-pump inhibitor (PPI) therapy is recognized as an anti-inflammatory treatment option for patients with EoE, able to reduce symptoms and eosinophilic infiltration. Recent research has suggested that PPI will have limited impact on subepithelial EoE processes such as fibrosis, because lack of inhibition of Th2 cytokine-stimulated eotaxin-3 expression by esophageal fibroblasts.

Aims & Methods: To investigate the potential effect of PPI therapy in reducing endoscopic features of EoE and in reverting fibrotic features after a short-term course. Data on the effectiveness of PPI to induce remission of EoE were collected from EoE CONNECT, a multicenter, prospectively-maintained registry of patients with EoE. Patients who received PPI therapy to induce EoE remission either as initial therapy or after failure to a previous dietary or drug-based option were included in the study. Patients who were under esophageal dilation were excluded. Clinical remission was defined by a decrease of >50% in Dysphagia Symptom Score; histologic remission was defined as a peak eosinophil count below 15 eosinophils per high-power field (eos/hpf). EREFS was scored by the severity of

5 endoscopic findings at baseline endoscopy and after a short course of PPI drugs. Changes in EREFS overall score and fibrotic subscore (presence of rings and/or strictures) were compared between EoE responders and non-responders to PPI treatment by t-test analyses. The potential additional benefit of achieving deep esophageal remission (<5 eos/hpf at post-treatment endoscopy) was also investigated.

Results: Data on 169 patients with EoE who received PPI therapy to induce remission of EoE and have registered information on clinical, histologic and endoscopic findings before and after PPI therapy were analyzed. Double dose of PPI were used in most cases (88%). At baseline endoscopy, 96 patients presented rings and 26 esophageal strictures. Eighty seven patients (51.5%) accomplished for histologic remission and symptomatic response together and were considered as PPI-responders. Mean±SD overall EREFS score at baseline were not different for PPI responder and non-responder patients, but reduced significantly only in PPI responders (2.59±1.73 to 1.06±1.01, p< 0.001), with no changes found among no responders (2.85±1.68 to 2.16±1.86). PPI responder associated to reduction from baseline in mean±SD rings' subscore (0.74±0.85 vs. 0.41±0.62; p=0.001) and strictures' subscore (0.10±0.29 vs. 0.01±0.11; p=0.007). Overall, the combined fibrotic score was significantly lower from baseline in EoE patients who responded to PPI therapy compared to those who did not (being 2.16 ±2.00 vs 1.28±1.08; p=0.009). Deep histologic remission provided no significant additional reductions of rings' and strictures subscores from baseline compared with partial histological remission (5-15 eos/hpf), but the combined fibrotic score showed a near-significant decrease (1.43±1.25 vs. 0.93±0.89, p=0.05).

Conclusion: Effective PPI therapy for EoE associates to significant endoscopic improvement overall, and reduces significantly endoscopic features of esophageal fibrosis in the short term. Deep histologic remission tended to produce increased benefits.

Disclosure: Nothing to disclose

P0087

DUPILUMAB NORMALIZES EXPRESSION OF GENES ASSOCIATED WITH TYPE 2 INFLAMMATION IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is chronic type 2 inflammatory disease resulting in eosinophilic inflammation of the esophagus, remodeling, and barrier dysfunction. Patients with EoE have an altered esophageal transcriptome compared with healthy controls, including changes in genes associated with type 2 inflammation, eosinophils, and mast cells. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4 and IL-13, key and central drivers of type 2 inflammation in multiple diseases. In a double-blind, placebo-controlled, phase 2 study (NCT02379052), adults with active EoE were randomized 1:1 to receive 12 weeks of subcutaneous dupilumab 300 mg weekly or placebo. Dupilumab significantly improved dysphagia and histological and endoscopic measures of disease with an acceptable safety

profile. This analysis assessed the effect of dupilumab on the expression of type 2 inflammatory genes in patients enrolled in the EoE phase 2 study. **Aims & Methods:** Pinch biopsies were collected from proximal, mid, and distal esophagus at baseline and Week 12 of 41 patients, and RNA was extracted for transcriptome sequencing. Mean gene expression of the 3 esophageal regions for each patient was examined at baseline and Week 12, then compared across patients with the published EoE and healthy transcriptomes. A relative change from baseline of ≥ 2 -fold, $q < 0.05$ was considered significant, reflecting appropriate adjustment for multiple testing.

Results: Overall, dupilumab 300 mg weekly modulated 1,302 genes, with very similar transcriptomes in all 3 analyzed esophageal regions. Dupilumab significantly normalized the expression of genes associated with type 2 inflammation. This includes genes associated with type 2 inflammatory cell responses (e.g. *CCR4*, *POSTN*, and *ALOX15*), proinflammatory cytokine production (e.g. *SPINK7*), and mucins (e.g. *MUC5B*). Dupilumab also significantly normalized genes associated with eosinophils and mast cells, by downregulating genes associated with eosinophil recruitment (e.g. *CCL26* and *CCR3*) and genes encoding eosinophil (e.g. *SIGLEC8*) and mast cell surface proteins (e.g. *IL1RL1*), which are all dysregulated in the EoE transcriptome. The post-dupilumab transcriptome more closely resembled that of healthy controls than the published EoE transcriptome. No changes in gene expression in the placebo group met significance thresholds.

Conclusion: In this phase 2 study, dupilumab reversed the EoE disease transcriptional signature, and normalized multiple genes associated with type 2 inflammation, eosinophils, and mast cells. This confirms the congruence of the mechanism of action of dupilumab and the mechanism of disease, highlighting the IL-4/IL-13 pathway as a central mediator of EoE pathogenesis.

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P0088

ACHALASIA AND OBSTRUCTIVE MOTOR DISORDERS ARE NOT UNCOMMON IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic disease that has been associated with various esophageal motility disorders, ranging from hypo- to hyper- contractile motility abnormalities. Recently, a potential association has been reported between eosinophilic esophagitis (EoE) and achalasia and other obstructive motor disorders.

Aims & Methods: We aimed to estimate the incidence of overlap between EoE and obstructive motor disorders including achalasia in a large cohort of consecutive EoE patients who underwent HRM as part of the initial evaluation. Furthermore, we aimed to assess the clinical course of both diseases and determine response to treatment.

We included consecutive patients with a new diagnosis of EoE who underwent HRM during initial evaluation at academic institutions in Padua, Genoa, Pisa and Naples, between 2012 to 2019. Demographic, clinical, endoscopic and histological characteristics were recorded at baseline and during management. EoE and esophageal motility disorders were diagnosed according to established international criteria. Treatments offered included proton pump inhibitors and topical steroids for EoE, pneumatic dilation and myotomy for achalasia.

Results: Of 109 consecutive patients (mean age 37 years, 82 male), 68 (62%) had normal HRM. Among 41 patients with motor disorders, 24 (59%) had minor motor disorders while 17 (41%) major motor disorders (including 8 with achalasia: type 1=1 patient, type 2=4 patients, and type 3=3 patients). Achalasia and non-achalasia obstructive motor disorders (DES=1 patient, jackhammer esophagus=2 patients, EGJOO=5 patients) had 14.7% prevalence in EoE. Achalasia was more frequent in females, with longer diagnostic delay and abnormal esophagogram ($p < 0.05$) compared to EoE without achalasia or obstructive motor disorders. Clinical features and endoscopic findings were similar between EoE patients with or without achalasia and obstructive motor disorders ($p=ns$); on the contrary, abnormalities on esophagogram were seen more often in achalasia and obstructive motility disorders ($p < 0.001$). Achalasia patients resembled those with other obstructive motility disorders, with no differences in demographic features, symptoms, endoscopic and histologic characteristics ($p=ns$) but they present a longer diagnostic delay ($p=0.038$). Concerning therapies, while there were no differences in PPI response between patients with achalasia and obstructive motility disorders and the other ones ($p=0.104$), the former re-

sponded less well to topical steroids ($p=0.005$). No differences in response to PPI and topical steroids between achalasia and other obstructive motor disorders ($p=1$ and $p=0.592$, respectively) were found. Invasive endoscopic or surgical treatments were required for symptom relief in 50% of patients with achalasia and obstructive motor disorders. After mean follow-up of 30 months, clinical, endoscopic and histological benefit from therapy was observed in 15 of 16 (94%) patients with achalasia and obstructive motor disorders. Only one patient with DES had persistent dysphagia and eosinophilic inflammation, likely related to noncompliance.

Conclusion: Achalasia and obstructive motor disorders are not uncommon in EoE, suggesting a potential causal link between these disorders. HRM is of value in patients with suspected EoE during the initial diagnostic work-up.

Disclosure: Nothing to disclose

P0089

ESOPHAGEAL MUCOSA INNERVATION IN PAEDIATRIC EOSINOPHILIC ESOPHAGITIS

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Introduction: The mechanism for symptom generation in eosinophilic oesophagitis (EoE) is not completely clear. Together with mechanical obstruction due to decreased oesophageal wall distensibility, oesophageal hypersensitivity has been noted. Hypersensitivity can be due to impairment of mucosal integrity and/or sensitization of mucosal nerves.

Aims & Methods: The aim of our study was to delineate the mucosal innervation in the proximal and distal oesophagus in paediatric EoE and control subjects and correlate this with the histological findings.

We prospectively recruited children undergoing an upper GI endoscopy for clinical reasons and identified a subgroup with normal histology +/- normal impedance pH-metry that served as controls and a patient group with histologically confirmed EoE. We obtained oesophageal biopsies from 3-5cm above the lower oesophageal sphincter and from the proximal/upper third. The biopsies were immunohistochemically stained for CGRP and TRPV1. CGRP positive nerve fibres were identified and their position relative to the lumen was determined (expressed as median number of cell layers from the lumen for all sections examined). The peak eosinophilic count per high power field (HPF) was used as proxy of disease activity in EoE.

Results: 19 children were included (12M:7F, median age: 11 years) in the control group and 12 in the EoE group (9M:2F, median age: 12 years). In the control group, CGRP positive nerve fibres were identified at a median of 19.5 cell layers from the lumen in the proximal and 19 cell layers in the distal oesophagus (Image 1). In the EoE group, CGRP positive nerve fibres were identified at a median of 14 cell layers in the proximal and 12.6 cell layers in the distal oesophagus ($p=0.0009$ and 0.01 respectively). There is a weak correlation between the number of eosinophils per HPF and the position of the nerve fibres in the oesophageal mucosa ($r=-0.46$). None of the nerve fibres identified expressed the TRPV1 receptor.

Conclusion: The oesophageal mucosa innervation in children with EoE is similar in the proximal and distal oesophagus with more superficial lying nerve fibres compared to controls. The superficiality of the nerve fibres may be driven by the underlying inflammation. These findings may contribute to the oesophageal hypersensitivity noted in EoE despite histological remission.

Disclosure: Nothing to disclose

P0090

ACID SUPPRESSANT MEDICATIONS AND EOSINOPHILIC ESOPHAGITIS: ARE THEY FRIENDS OR FOES?

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Introduction: Eosinophilic esophagitis (EoE) is an atopic-immune mediated, inflammatory process isolated to the esophagus leading to symptoms of esophageal dysfunction. Treatments are elimination diets, topical steroids, and proton pump inhibitors (PPI). A recent report suggests that acid suppression therapy (AST) with PPI and histamine-2 receptor antagonist (H2RA) exposure during infancy is a risk factor for EoE.

Aims & Methods: To investigate whether AST at any age is associated with an increased risk of EoE.

Data were obtained from a commercial medical database (IBM Explorys Solutions, IBM, Inc.) that has patient information from 27 U.S. healthcare networks from 1999 to present. Patients who underwent esophagogastroduodenoscopy (EGD) were identified using Systematized Nomenclature of Medicine - Clinical Terms (SNOMED-CT). Cases were defined as patients who underwent an EGD and started AST (PPI or H2RA) for the first time after at least 90 days from the initial EGD for a period of three months then underwent a second EGD and were subsequently diagnosed with EoE. Controls were patients who underwent an EGD and never received AST. Patients with a pre-existing diagnosis of EoE or previously received AST were excluded from the analysis. The 90-day period after the initial EGD was used to exclude patients who received AST prior to the final diagnosis of EoE (based on a past clinical guideline to exclude PPI-responsive eosinophilia). Odds ratio (OR) and 95% confidence interval (CI) for the OR were calculated for the association of AST and development of EoE.

Results: 2,225,060 (3.5%) of individuals (64,417,480) within the database underwent an EGD.

The overall population prevalence of EoE was 5 in 10,000 (32,220 cases), this is consistent with previous population studies. The risk of being diagnosed with EoE in a patient who never received AST (controls) was 0.37%. Compared to controls (Table 1), those who received any AST had a 1.2 (CI: 1.1 - 1.3) times higher odds of having a new diagnosis of EoE; those who received PPIs had a 1.6 (CI: 1.5 - 1.7) higher odds; and individuals who received H2RAs did not have an increased risk of EoE (OR: 1.1, CI: 0.9 - 1.4). Receiving both ASTs conferred a 3.0 (CI: 2.7 - 3.2) higher odds of being diagnosed with EoE compared to controls. Subgroup analysis (Table 1) comparing both and any ASTs to individual PPI/H2RA revealed the effect of H2RAs to be minimal when used alone and additive if combined with PPIs.

	Cases N (Risk %)	OR	95% CI
EGD + no AST's (Controls)	2130 (0.37%)		
EGD + H2RA only	80 (0.41%)	1.12	0.90 - 1.41
EGD + PPI only	1680 (0.58%)	1.60	1.50 - 1.70
EGD + Both AST's (H2RA and PPI)	650 (1.08%)	2.97	2.72 - 3.24
EGD + Any AST's (H2RA or PPI)	1720 (0.44%)	1.18	1.11 - 1.26
EGD + Both AST's (H2RA and PPI) vs H2RA only		2.64	2.10 - 3.33
EGD + Both AST's (H2RA and PPI) vs PPI only		1.87	1.71 - 2.05
EGD + Any AST's (H2RA or PPI) vs H2RA only		1.05	0.84 - 1.32
EGD + Any AST's (H2RA or PPI) vs PPI only		0.75	0.70 - 0.80

[Table 1: Main Analysis and Subgroup Analysis]

Conclusion: Although PPIs are a treatment for EoE, our findings suggest the use of a PPI at any age is a risk factor for the development of EoE. H2RA therapy alone is not a risk for EoE. However, the use of both ASTs increases the risk over PPI therapy alone. This effect might be due to more severe symptoms in EoE patients leading to more aggressive therapy. The pathophysiology for this increased risk of EoE is unclear.

Disclosure: Nothing to disclose

P0091

ANTI-TUMOR NECROSIS FACTOR THERAPY AND EOSINOPHILIC ESOPHAGITIS: IS THERE ANY CONNECTION?

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Introduction: Eosinophilic esophagitis (EoE) is an atopic-immune mediated, inflammatory process isolated to the esophagus leading to symptoms of esophageal dysfunction. Eosinophilic esophagitis has been increasingly reported to be associated with other immune mediated disorders (IMD). It is unknown whether this association is due to a common underlying immune dysregulation or due to other factors associated with IMDs. We hypothesized that anti-tumor necrosis factor- α therapy (anti-TNF) is one of the IMD associated factors leading to the development of EoE.

Aims & Methods: To investigate whether anti-TNF therapy is a risk factor for EoE.

Data were obtained from a large commercial medical database (IBM Explorys Solutions, IBM, Inc.) that contains patient information from 27 U.S. healthcare networks from 1999 to present. Systematized Nomenclature of Medicine - Clinical Terms (SNOMED-CT) were used to extract patient information. We defined cases as patients without a pre-existing diagnosis of EoE who had an office visit (index event) and subsequently received an anti-TNF (etanercept, adalimumab, or infliximab) regardless of indication. We defined the comparator group as those who had a diagnosis of EoE and never received an anti-TNF. We performed subgroup analyses for inflammatory bowel disease (IBD) and other immune mediated diseases (rheumatoid arthritis, ankylosing spondylitis, psoriasis, Behcet's syndrome, hidradenitis suppurativa, and uveitis) and for individual diagnoses (only those diseases with sufficient numbers in the database were analyzed). Odds ratio (OR) and 95% confidence interval (CI) were calculated for the association of anti-TNF therapy and the development of EoE.

Results: 135,630 (0.21%) of all patients (64,417,480) within the database were prescribed an anti-TNF. Cases (those prescribed an anti-TNF for any indication) had a 2.22 (CI: 1.92 - 2.56) higher odds of being diagnosed with EoE compared to controls who never received an anti-TNF (Table 1). Cases with IBD had a 1.84 (CI: 1.1 - 2.25) higher odds of having EoE when compared to patients with IBD who never received anti-TNF therapy. Cases with other IMDs had a 1.65 (CI: 1.32 - 2.06) higher odds of developing EoE when compared to those with an IMD and never prescribed an anti-TNF (Table 1). Cases with Crohn's disease (OR: 1.94, CI: 1.48 - 2.52), rheumatoid arthritis (OR: 1.69, CI: 1.24 - 2.27), and psoriasis (OR: 1.95, CI: 1.39 - 2.73) had a higher odds of developing EoE as compared to controls. Ulcerative colitis (OR: 1.02, CI: 0.51 - 1.86) and ankylosing spondylitis (OR: 1.49, CI: 0.73 - 3.05) did not have higher odds of EoE (Table 1).

Conclusion: The initiation of an anti-TNF in patients with IMD was associated with an increased occurrence of EoE in our population. The underlying pathophysiologic mechanism of this increased risk of anti-TNF therapy requires further investigation.

Disclosure: Nothing to disclose

	Cases N (Risk %)	Comparator N (Risk %)	OR	95% CI
All patients	190 (0.17%)	20850 (0.07%)	2.22	1.92 - 2.56
IBD	110 (0.31%)	740 (0.17%)	1.84	1.51 - 2.25
Other IMD	90 (0.12%)	620 (0.07%)	1.65	1.32 - 2.06
Ulcerative colitis	10 (0.15%)	170 (0.15%)	1.02	0.51 - 1.86
Crohn's disease	70 (0.34%)	260 (0.18%)	1.94	1.48 - 2.52
Rheumatoid arthritis	50 (0.10%)	280 (0.06%)	1.69	1.24 - 2.27
Ankylosing spondylitis	10 (0.15%)	30 (0.10%)	1.49	0.73 - 3.05
Psoriasis	40 (0.15%)	210 (0.08%)	1.95	1.39 - 2.73

[Table 1: Association of anti-TNF therapy and development of EoE in immune-mediated diseases]

P0092

MENTAL DISTRESS AMONG ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Data on the prevalence of mental distress among adult eosinophilic esophagitis (EoE) patients are scarce. Also, a significant gap remains in understanding of the degree to which clinical and socio-demographic variables are related to significant psychological symptoms.

Aims & Methods: Adult EoE patients were invited to complete standardized measures on anxiety and depressive symptoms (HADS) and general psychopathology (SCL-90-R). All scores were compared to General Population (GP) norms, stratified by age and sex. Socio-demographic and clinical factors were assessed by means of a self-reported questionnaire. Factors with p-value < 0.2 in univariate analysis, or factors that were considered clinically relevant, were entered into a multivariate logistic regression model.

Results: In total, 147 adult EoE patients (61% males, median age 43 (IQR 29 - 52) years were included (response rate 71%). No difference with GP values was found for total anxiety and depressive symptoms (7.8 $\pm$ 6.6 vs 8.3 $\pm$ 0.21; P = 0.35). A total of 38/147 (26%) patients reported high levels of anxiety and/or depressive symptoms (HADS-A: 35/147 (24%) and HADS-D: 14/147 (10%) $\geq$ 8), indicative of a psychiatric disorder. In a multivariate analysis, age between 18-35 years was independently associated with high levels of anxiety ($\geq$ 8 HADS-A) (OR 3.0 | 95 % CI 1.307 - 6.881; P = 0.01) The SCL-90-R Global Severity Index (GSI) was significantly higher compared to the GP (P < 0.001). Also the dimensions; depression, somatization, insufficiency of thinking and acting, hostility, sleep disturbance, anxiety and sensitivity were all significantly higher compared to the GP (P < 0.05). In total, 43 (29%) patients reported to have current or past mental problems, of which 23 (53%) felt it was related to EoE.

Conclusion: A considerable prevalence of mental distress was observed in adult patients with EoE, with a 3-fold risk of features of significant anxiety in those patients younger than 35 years. Therefore, a pro-active approach in the management of EoE towards these symptoms seems warranted.

Disclosure: Nothing to disclose

P0093

EOSINOPHILIC OESOPHAGITIS - CLINICAL, ENDOSCOPIC AND HISTOLOGICAL SCORING SYSTEMS IN INITIAL DIAGNOSIS AFTER REMISSION INDUCTION AND IN REMISSION MAINTENANCE UNDER TOPICAL CORTICOSTEROIDS

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Introduction: Eosinophilic oesophagitis (EoE) is a chronic inflammatory, allergenic/immune-mediated disease of the esophagus. EoE is characterized clinically by symptoms of esophageal dysfunction and histologically by an eosinophil-predominant inflammation restricted to the esophagus. Clinical (Straumann Dysphagia Index, SDI), endoscopic (EREFS) and histological (EoE-HSS) scoring systems exist to determine disease activity. Topical corticosteroids (tCS) are effective in inducing clinico- histological remission (RI) and maintenance of remission (RM) in active EoE. However, often symptoms, endoscopic and histological findings do not correlate.

Aims & Methods: Correlation of SDI, EREFS and EoE-HSS at initial diagnosis (ID) of EoE, after RI and in RM with tCS among each other as well as in the course of therapy.

Retrospective cohort analysis of 2006-2020 in patients with active EoE with follow-up intervals up to 6 years. SDI, EREFS and EoE-HSS were collected at the time of ID, after RI and during RM (*Definition: remission: ≤ 15 Eos/HPF and reduction SDI ≥ 3*). The evaluation based on descriptive statistics, Friedman test and Bonferroni-adjusted post-hoc comparisons.

Results: At the time of RI, all scores were analyzed in 29 of 60 patients (62% male, mean age 48). All EoE patients were treated with tCS for a mean of 13 weeks until RI. 19 complete data sets were evaluated in RM after a mean duration of therapy with tCS of 21 months. The EREFS showed significant correlations to EoE-HSS in RI (Spearman correlation $r=0.56$; $p=0.013$) as well as in RM ($r=0.61$; $p=0.006$). The pairwise comparison using Bonferroni-adjusted post-hoc tests reveals significant differences between ID and RI for SDI ($r=-0.035$; $p<0.001$) and EoE-HSS ($r=0.268$; $p=0.028$), but not for EREFS. No statistical significance of the three scores was detected between RI and RM.

Conclusion: Clinical, endoscopic and histological scores to determine activity in EoE do not correlate at time of ID.

The comparison of the respective scoring systems after induction therapy reveals significant differences at the time of ID and RI symptomatically and histologically, but not in RM under tCS therapy.

These results underline the effectiveness of tCS in RI and RM therapy of active EoE.

Disclosure: Nothing to disclose

P0094

LONG-TERM TREATMENT WITH PROTON PUMP INHIBITORS AND TOPICAL STEROIDS IN EOSINOPHILIC ESOPHAGITIS: EFFICACY AND FACTORS INFLUENCING RESPONSE

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Introduction: Eosinophilic esophagitis (EoE) is a chronic disorder. While induction therapy is well defined, evidence about long-term management and factors influencing the course of the disease are still lacking.

Aims & Methods: The aim of this study was to evaluate the long-term outcome of EoE patients who started proton pump inhibitors (PPIs) or topical steroids as induction therapies. Prospectively collected data from 58 EoE patients (42 Male, mean age at diagnosis 33yo), with a mean follow-up of 2 years and 10 months, were analysed. All patients had symptoms suggestive of EoE (i.e. dysphagia and bolus impaction) and after endoscopic/histological confirmation of EoE were treated with high-dose PPI therapy. In case of eosinophilic infiltration persistence at 8-weeks upper endoscopy, treatment with topical steroids was started. Thereafter, patients repeated the upper endoscopy to confirm the histological remission (i.e. eosinophilic peak < 15 /HPF). During follow-up, 3 different patterns of therapeutic response were identified: continuous responders (CR; histological remission in more than 75% of endoscopic evaluation carried out every year from the diagnosis), intermittent responders (IR; remission in 25-75% of endoscopic evaluations), non-responders (NR; remission in less than 25% of endoscopic assessments). Risk factors for relapse were calculated.

Results: Seventeen (29%) patients achieved clinical and histological remission using PPI (PPI-R), 32 (56%) responded to topical steroids (TS-R), 3 (5%) to diet and 6 did not respond to any therapy (10%). Remission was durable in 60% of PPI-R patients who maintained maximal dose therapy, and in 58% of those attempting a tapering. Among TS-R patients, remission was maintained in 56% of those taking maximum dosage and in 50% of those who tapered. No significant difference in maintenance of remission between those who tapered therapy (PPI or TS) and those who did not, was observed ($p=0.633$ and $p=0.912$). No different risk of relapse between who tapered and who did not, both for PPI ($p>0.99$, OR=2, I=0.24-29.80) and for TS ($p=0.38$, OR=2.25, I=0.46-10.61), emerged. In terms of long-term efficacy, 64% were CR, 26% were IR, 10% NR. Considering CR, IR and NR, there was a significant difference in terms of age at diagnosis and diagnostic delay ($p=0.044$ and 0.011 , respectively). The mean age at diagnosis was 36yo for CR, 30yo for IR and 20yo for NR. Diagnostic delay was 3years and 6months for CR, 2 years and 7 months for IR, 8years and 7months for NR.

Conclusion: Our data demonstrated that PPI and TS are effective therapies to induce remission and to maintain histological response in the long term in most patients (90%), even after tapering. Only a small proportion of patients do not respond to available treatments. Characterization of these patients could help, in the future, to improve therapeutic outcome.

Disclosure: Nothing to disclose

P0095

SERUM BIOMARKERS IN THE DIAGNOSTICS OF PATIENTS WITH SUSPECTED EOSINOPHILIC ESOPHAGITIS - PRELIMINARY REPORT

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Introduction: Invasive diagnostic tests monitoring the effectiveness of eosinophilic esophagitis (EoE) therapy, i.e. according to current standards, periodic panendoscopy with specimens for histopathological examinations, encourage the search for alternative, less invasive methods suggesting broadening the diagnosis leading to diagnosis, but also monitoring the course of the disease. In the light of previous studies, we do not have a biomarker of blood serum with sufficient diagnostic accuracy.

Aims & Methods: The aim of the study is to assess the correlation of serum biomarkers concentration with the diagnosis of EoE. To date, 56 people have been studied, each of whom had serum levels of interleukin 5 (IL-5) and 13 (IL-13), transforming growth factor beta 1 (TGF-β1), eotaxin 3, as well as panendoscopy with specimens collection from the esophagus for histopathological examination. The criteria for diagnosing EoE according to the current UEG, EAACI ESPHAGAN and EUREOS guidelines (2017) and Updated international consensus diagnostic criteria of the AGREE conference (2018) was esophageal biopsies of ≥15 eosinophils per high-power field, in co-occurrence of esophageal dysfunction symptoms and absence of other causes of esophageal eosinophilia. Patients who did not meet these criteria constituted the control group. Quantification of biomarkers was performed using an enzyme immunoassay (ELISA). In data analysis, $p < 0.05$ was considered statistically significant.

Results: Only 15 people with dysphagia symptoms and suspected EoE were diagnosed with the disease (26,79%). The median TGF-β1 concentration was significantly increased in patients with EoE compared to the control group [11025,00 pg/ml (interquartile range - IQR: 7170,00-14100,00) vs. 7839,00 pg/ml (IQR: 6297,00-9195,00), $p = 0,022$], the median eotaxin 3 concentration was on the upper limit of significance [96,00 pg/ml (IQR: 43,80-182,00) vs. 50,00 pg/ml (IQR: 27,70-100,40), $p=0,054$], while for the other markers no statistical significance was obtained: IL-13 [2,50 pg/ml (IQR: 1,28- 3,30) vs. 3,70 pg/ml (IQR: 1,45-5,00), $p=0,185$], IL-5 [4,07 pg/ml (IQR: 3,60-7,10) vs. 4,30 pg/ml (IQR: 3,30-5,90), $p=0,452$].

Conclusion: The increase in serum TGF-β1 concentration correlates with the diagnosis of EoE, which suggests a potential role in recognizing, and perhaps also controlling the course of the disease. Due to the small group of patients and promising results of analyzes, it seems advisable to continue the study, further recruitment of participants, inclusion of additional biomarkers in the determinations, as well as to continue to observe changes in their concentrations during EoE therapy. From the obtained data, in further analysis, it is advisable to develop, among others decision tree, which can be a tool supporting the diagnosis, monitoring and forecasting of the course of EoE in clinical practice, not on the basis of the concentration of individual biomarkers, but their group and interrelationships.

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P0096

DEFINING AN EOSINOPHILIC LEUKOCYTE COUNT PER MM² THRESHOLD FOR THE DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS USING A DIGITAL PATHOLOGY PLATFORM

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, antigen-mediated disease causing severe dysphagia. Diagnosis relies on clinical symptoms and eosinophilic leukocyte count (EoL) per High Power Field (HPF). However, histology samples frequently may not fill the whole objective and there is an almost 2.5-fold difference in HPF area of different microscopes. Thus, a standardized number of EoL/mm² may decrease diagnostic discrepancies and may facilitate better diagnostic rate.

Aims & Methods: Our aim was to analyze EoL/mm² and other histopathologic features in EoE using a digital pathology platform, and compare these to gastroesophageal reflux disease (GERD) to define a EoL/mm² threshold for the diagnosis of EoE.

45 EoE and 45 matched GERD cases were selected retrospectively from the archives of the Pathology Departments of Semmelweis University, Budapest, Hungary. Clinicopathological data were collected, slides were digitalized using *Pannoramic™ P250 Flash* digital slide scanner (3DHISTECH Ltd., Budapest, Hungary) and re-analyzed by 2 independent GI histopathologists. Epithelial and subepithelial compartments and EoLs were annotated digitally with *CaseViewer*.

Results: 45 EoE patients were 66% males; mean age was 23.5 ± 19.7 years. Most common endoscopic manifestations were rings (36.8%) and longitudinal furrows (21.1%). Histopathologic EoE findings were: eosinophilic cell degranulation 86.6%, spongiosis 75.5%, eosinophilic aggregate formation 66.7%. Average sample areas were similar in both groups, whereas digital image analysis showed significantly higher EoL/mm² count in both epithelial (171.2 ± 177.2 vs 3.3 ± 11.6) and subepithelial (61.1 ± 67.11 vs 4.5 ± 13.22) compartments of EoE as compared to GERD cases. ROC analysis found a reliable threshold for differentiating EoE from GERD at 33 EoL/mm² (AUC=0.993) in the epithelial and 16 EoL/mm² in the subepithelial compartment (AUC=0.882).

Conclusion: In 2018 a consensus paper of international experts suggested an estimated 60 EoL/mm² threshold for diagnosing EoE instead of 15 EoL/HPF. Our study with numerical counting of EoLs on a digital platform found that a lower, 33 EoL/mm² threshold might be reliably differentiate EoE from GERD. Further prospective studies are needed to validate these findings.

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P0097

ENDOSCOPIC AND RADIOLOGICAL ABNORMALITIES ARE COMMON IN PATIENTS WITH EOSINOPHILIC OESOPHAGITIS AND ARE MORE LIKELY WITH INCREASED OESOPHAGEAL SAMPLING - A SINGLE CENTRE LONGITUDINAL EXPERIENCE

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Introduction: Eosinophilic Oesophagitis (EoE) is a chronic allergic disorder of the oesophagus, associated with an inflammatory infiltrate of eosinophils into the oesophagus, and associated with submucosal fibrosis and dysphagia. A high index of suspicion is needed at endoscopy and targeted biopsies from areas of mucosal abnormality in addition to standard multiple level sampling strategies, yielding the best results.

Aims & Methods: We aimed to evaluate the endoscopic, pathologic and radiologic features of patients with EoE over a 3-year investigative period. A retrospective study of patients with a pathological diagnosis of eosinophilic oesophagitis between 2015 - 2017 was undertaken following a data extraction of results using the Electronic Patient Record (EPR) system. Baseline characteristics were interrogated, in addition to endoscopic findings, associated radiological abnormalities, management strategies and patient outcomes.

Data was extracted and analysed using Rstudio.

Results: A total of 225 patients with a new diagnosis of EoE were made during the time period studied. Median age distribution was 25-30 years, with the oldest patient diagnosed at 75-years of age. The main indication for endoscopy was dysphagia (47%), followed by odynophagia (27%). Food bolus obstruction was present in 25 individuals (11%). The most common endoscopic finding was stricture (40%). A normal oesophagus was described in 18% of individuals with trachealisation seen in 15% of cases. A schatzki ring was present in 10% of cases with endoscopic evidence of oesophagitis described in 45%.

Eosinophil counts ranged from 15-72 eos/hpf with furrows and exudates associated with higher mean eosinophil counts/hpf (55 and 52 respectively) than other endoscopic features, and mucosal oedema associated with lower counts (mean 32 eos/hpf).

Number of biopsies taken ranged from 1-20. Taking more biopsies was associated with a higher chance of spongiosis as well as fibrosis being commented on during histopathological analysis ($p < 0.001$ and $p = 0.013$ respectively).

Conclusion: Eosinophilic Oesophagitis is becoming an increasingly more commonly diagnosed condition and is associated with significant patient morbidity. Heightened awareness of endoscopic features of disease as well as enhanced biopsy protocols maximise the chances of successful diagnosis.

Disclosure: Nothing to disclose

P0098 WITHDRAWN

P0099

GASTROESOPHAGEAL REFLUXES DEPEND ON NUTRIENTS CONSUMPTION IN CHILDREN

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Introduction: In contrast to adults, association of number and types of gastroesophageal refluxes with usual nutrients consumption is not widely studied in children.

Aims & Methods: The aim of the study was to evaluate the correlation between types and number of gastroesophageal refluxes and nutrients consumption in children and adolescents.

The study was approved by IEC. The data of examination of 219 children (7-17 y.o.), 147 with GERD and 72 controls served as a source for the study. The amount and types of GER were determined using 24-hours esophageal pH-impedansometry (Ohmega, MMS, The Netherlands). Food frequency questionnaire was used to evaluate level of nutrients consumption. To make possible comparison of data obtained in different age and sex groups of children, direct levels of nutrients consumption were converted to a percentage deviation from the recommended daily allowance rates. Spearman rank correlation analysis was performed with the use of Statistica 10 (StatSoft Inc., USA) to clear out whether association exists between usual nutrition and number of gastroesophageal reflux episodes, their acidity and duration in children.

Results: Statistically significant ($p < .05$) correlation of Acid exposure time was found with amounts of PUFA (Spearman $R = -0.334$), ω -3 ($R = -0.33$), ω -6 ($R = -0.3$); retinols ($R = -0.34$), niacin ($R = -0.28$) and ascorbic acid ($R = -0.37$) consumption.

The number of acid refluxes correlated with energy values of the ration ($R = 0.269$), amount of total protein ($R = 0.279$), total fat ($R = 0.272$), total carbohydrates ($R = 0.152$), and added sugar ($R = 0.157$) consumption.

The number of weak-acid refluxes was not correlated with any of the parameters of actual nutrition.

We found significant correlation between the number of non-acid refluxes and amount of PUFAs ($R = 0.19$), ω -6 ($R = 0.151$), ω -3 ($R = 0.19$); sodium ($R = 0.158$), phosphorus ($R = 0.166$), vitamin B1 ($R = 0.17$), niacin ($R = 0.19$), and ascorbic acid (0.23).

Conclusion: We found that types and number of gastroesophageal refluxes, as well as acidification of the lower part of oesophagus may be associated with usual nutrition. Our results may mean that different nutrients have different impact on esophageal motility in children. The results may have practical outcome for planning non-pharmacological intervention in children with GER.

Disclosure: Nothing to disclose

P0100 WITHDRAWN

P0101

EPITHELIAL PERMEABILITY AND INFLAMMATORY PROCESS OF ESOPHAGEAL MUCOSA AFTER ANTI-REFLUX SURGERY IN PATIENTS WITH GASTRO-ESOPHAGEAL REFLUX DISEASE

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Introduction: Two major injury mechanisms among others proposed for causing mucosal damage in esophageal epithelium of patients with gastroesophageal reflux disease (GERD); gastric acid, pepsin, other noxious agents, and cytokine-mediated inflammation. Laparoscopic anti-reflux surgery (LARS) has restrain reflux effectively and symptoms rapidly disappear. Therefore, LARS patients are the most effective model to study esophageal mucosa absence of harmful agents.

Aims & Methods: We aim to evaluate the tissue resistance and inflammatory process of esophageal mucosa of the cases before and after LARS and compare with healthy controls (HC) in order to understand the underlying pathophysiologic mechanism of GERD.

Upper GI endoscopy, esophageal high resolution manometry, 24h pH-MII monitoring were performed in all patients. Nine esophageal biopsies from 22 patients pre- and post- LARS (13 men; 42,9 ± 11,5 years), 23 healthy controls (7 men; 41,9 ± 10,8 years) were taken. Four biopsies used for Ussing chamber studies, three homogenized for inflammatory studies, rest for measure dilated intercellular spaces (DIS). Upper GI endoscopy and biopsies were repeated 3-4 months after LARS. All patients were symptom-free. Biopsies were analysed in Multiplex Immunoassay System (Bio-Plex®) to scan 40 chemokines and studied in Ussing chambers to measure transepithelial resistance (TEER) and tissue permeability with fluorescein diffusion.

Results: TEER results following LARS were significantly higher than HC and pre-LARS (Table). Additionally, HC were significantly increased compared to pre-LARS. Mucosal permeability of post-LARS was significantly decreased versus pre-LARS and HC. The levels of C-C Motif Chemokine Ligand (CCL-) 1, 3, 4, 7, 8, 17, 21, 24, 26, 27, interleukin (IL-) 1b, 10, C-X-C motif Chemokine Ligand (CXCL)-2,-6,-8 Interferon gamma (IFNG) and macrophage migration inhibitory factor (MIF) of post-LARS were increased compared to pre-LARS (p<0.05). IL-8 and TARC levels of pre-LARS was significantly higher than HC. DIS score of HC (0,97 ± 0,21 µm) was significantly lower (p<0.0001) than pre- and post-LARS. DIS of post-LARS (1,27 ± 0,26 µm) insignificantly decreased versus pre-LARS (1,32 ± 0,24 µm).

Conclusion: The TEER and permeability results implicate that LARS made very efficient recovery within esophageal epithelium resistance in patients with GERD even though higher than HC. Higher levels of anti-inflammatory chemokines (IFNG, IL-10 and CCL-7) and tissue healing markers (CCL-17, -22, IL-4, -10) may indicate the role of macrophages and neutrophils during recovery phase in post-LARS. Similar results of pre- and post-LARS patients for DIS measurements implicates that short-term recovery phase may not enough to indicate perceptible difference in tissue level or these changes might be irreversible.

We concluded that LARS improves the permeability of esophageal mucosa in short term follow-up possibly related with the assistance of anti-inflammatory chemokines (IFNG, IL-10 and CCL-7) and tissue healing markers. DIS might not recover at all or need long-term healing process to recover since we measured maximum of 4 months after surgery. To the best of our

knowledge, there is no study about epithelial permeability and inflammatory mechanisms together and before and after LARS, which is an ideal model for recovery of EE, there is a need for more data to evaluate pathogenesis of GERD.

Disclosure: Nothing to disclose

	HC	Post-LARS	Pre-LARS
TEER (Ohms)	176,9 ± 39,2 c	206,1 ± 40,7 a, b	151,0 ± 38,7
Permeability (pmols)	41,2 ± 16,3	29,7 ± 18,1 d, e	43,3 ± 19,2

a; p=0.0001 vs pre-LARS, b; p=0.031 vs HC, c; p=0.047 vs pre-LARS, d; p=0.028 vs pre-LARS, e; p=0.046 vs HC

[Table. Transepithelial resistance and permeability results of the groups]

P0102 WITHDRAWN

P0103

MICROSCOPIC ESOPHAGEAL INJURY CONTRIBUTES TO HEARTBURN PERCEPTION IN PATIENTS WITH GERD

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Introduction: Heartburn is the most prominent feature of GERD. Multiple receptors have been identified responsible for heartburn perception, with TRPV1 receptor activated by acid being best described. Intensity of heartburn, however, varies greatly among the patients as various pathophysiological mechanisms are involved. Although mucosal integrity plays a key role in the pathophysiology of GERD, its direct involvement in the perception of heartburn has not been established yet.

Aims & Methods: We hypothesized that the infusion of noxious stimuli into the esophagus induces heartburn of intensity that is proportionate to the mucosal integrity in patients with heartburn. TRPV1 activator acid (HCl solution, pH=1, 10 min.) was infused (8ml/min.) into the esophagus via a transnasal tube with the opening placed 5 cm above the manometrically determined LES. The intensity of sensations was recorded every 2 min. by visual analogue scale (VAS, range 0-10). 12 patients with chronic heartburn were included. All patients had 24 hour pH/impedance off PPI. We reviewed the pH impedance tracings and determined MNBI values as the average value of three 10 min. intervals (1:00, 2:00 and 3:00 a.m.) in the periods without reflux events and/or swallowing. We analyzed the correlation between the MNBI value and the dynamics of heartburn perception based on VAS.

Results: 12 subjects received acid infusion. Infusion induced heartburn in all patients. Maximal VAS score was 7.1±2.6 (N=12). 6 patients had positive pH/impedance study (AET>6%). In order to avoid the contribution of hypersensitivity in the heartburn perception we determined the dynamics of heartburn development. We defined it as the ratio between the intensity of heartburn in the 2. min. of the infusion (VAS) and the maximal intensity of heartburn (VAS). We obtained the MNBI values for 6 impedance segments and performed correlations between the dynamics of heartburn and MNBI values. Mean MNBI values were 2727±275Ω, 2841±289Ω, 2148±227Ω, 2244±266Ω, 2363±326Ω and 2274±316Ω in Z1-Z6, respectively. We observed significant correlation between the dynamics of heartburn (as determined by the ratio value) and the MNBI value in the most distal (Z6) impedance segment (R=0.7, p=0.01). No significant correlation

was found for MNBI values in Z1-Z5 (R values were 0.34, 0.39, 0.2, 0.24, 0.48, respectively, $p=NS$). Interestingly, correlations between the maximal VAS values and MNBI revealed no statistical significance (data not shown). **Conclusion:** Impaired mucosal integrity seems to directly contribute to heartburn perception in patients with chronic heartburn. Importantly, this relationship seems valid for the whole heartburn patients group (regardless of the degree of acid exposure). Rather the dynamics of heartburn development than the heartburn intensity itself is determined by the mucosal integrity.

Disclosure: Nothing to disclose

P0104 WITHDRAWN

P0105

EFFECT OF HIGH ACID EXPOSURE ON THE ESOPHAGUS IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE: PH-IMPEDANCE, CLINICAL AND ENDOSCOPIC PARALLELS

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Introduction: Gastroesophageal reflux disease (GERD) is common in children and has a varied clinical manifestation with a wide range of typical gastroesophageal and atypical extra-esophageal symptoms. pH-impedance testing makes possible the assessment of pH and other parameters of GERD together with disease symptoms and the diagnosis of GERD [1].

Aims & Methods: **Aim:** it was to assess the parallels between the clinical gastroesophageal reflux disease (GERD) - symptoms (typical and atypical), endoscopic findings and the data of the pH-impedance monitoring in pediatric patients with an abnormal esophageal reflux.

Methods: criteria for inclusion of patients in the study: the presence of GERD related symptoms (typical and/or atypical); abnormal esophageal reflux burden on the pH-impedance monitoring. Los Angeles classification was used to assess the endoscopy findings. The assessment of pH-impedance monitoring data performed from November 2017 till November 2019 revealed abnormal esophageal reflux burden in 93 patients (acid exposure time - AET > 7%, total number of reflux episodes > 70/100 - in children aged > 1 year/infants) [2-4].

Calculating the average AET in this group resulted in the index of 10.64 (CI% 9.46 - 12.11); 75% = 12.6 (CI% 11.3286 to 16.5000). For this reason AET = 11.33 was selected as the lower limit of the esophagus high degree of acidification.

The study included 27 patients with AET > 11.33%. Male - 18 (66.7%), female - 9 (33.3%), aged 1 - 17 years (average age = 6,37).

Male/female ratio = 18: 9.

Results: Based on the results of clinical symptoms and endoscopic findings the patients were divided into 5 groups: reflux esophagitis (RE) - 8, non-erosive GERD (NERD) - 11, eosinophilic esophagitis (EoE) - 1, esophageal atresia (EA) - 6, 3 of them have RE), polyp of the esophagogastric junction (EGJ) - 1.

Clinical symptoms:

- EA: typical symptoms - 2, atypical symptoms - 2, mixed - 2;
- RE: typical - 3, atypical - 2, mixed - 3;
- NERD: typical - 0, atypical - 9, mixed - 2;
- EoE: typical - 1;
- polyp of the EGJ: typical - 1.

Typical symptoms: heartburn, dysphagia, belching, vomiting, abdominal pain, nausea.

Atypical symptoms: cough, obstructive bronchitis, frequent pneumonia.

Clinical symptoms in general: typical - 6, atypical - 14, mixed - 7.

The Kruskal-Wallis test was performed in groups of patients with RE, NERD and EA. As a result of this test a significant difference revealed - $p = 0.011397$ in the duration of the longest reflux in the group with EA compared with the groups of RE and NERD - Post-hoc analysis (Dunn). No significant difference in indicators of AET, number of reflux episodes and age is revealed.

Conclusion: 1 - atypical symptoms prevail in the group of NERD;

2 - males mostly suffer from the abnormal esophageal reflux burden;

3 - the average duration of the longest reflux episode in the group with EA is significantly higher than in groups with NERD and RE.

Groups	Male/ female	age	AET (%)	Total number of reflux episodes	Duration of the longest reflux
RE	8/-	8,2 95% CI 4,4-11,9	18,11 95% CI 11,68-25,54	128,9 95% CI 46,3- 211,9	31,7 95% CI 22,9 - 40,5
NERD	5/6	6,1 95% CI 3,8-8,2	18,48 95% CI 13,62-23,34	64,3 95% CI 44,8-83,8	33,0 95% CI 26,9 - 39,1
EA	4/2	3,7 95% CI 0,2-7,6	21,28 95% CI 9,58-32,97	79,3 95% CI 25,1-133,6	82,0 95% CI 32,5 - 131,6
Polyp EGJ	-/1				
EoE	1/-				

[Demographic characteristics and pH-impedance data of patients with GERD.]

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Disclosure: Nothing to disclose

P0106

IMPACT OF THE MINIMUM DURATION OF THE REFLUX EPISODES IN PHMETRY IN THE REFERENCE VALUES

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Introduction: The minimum duration used in the analysis of reflux episodes in pHmetry varies considerably depending on the software and the recorders used. In older equipments, due to technical limitations, the minimum duration to consider an episode is 4-8 seconds for wired pHmetry and 6 seconds for wireless pHmetry. Modern equipment usually uses a sampling rate of 1 data per second and usually sets the minimum duration of episodes to 2 seconds. However, reference values are generally used without taking this variable into account, which modifies the results and their possible interpretation.

Aims & Methods: Objective: To determine the implications of the variability in the minimum duration to consider a reflux episode in the analysis of the pHmetry records.

Material and method: The pHmetry records, without eliminating the intake periods, of 10 control subjects and 20 patients with reflux were studied, applying values of minimum duration of one episode of: 2, 4, 6 and 8 sec. and the modifications of the acid exposure time (AET), generic score (GS) and its repercussion in the consideration of conclusive evidence of pathological reflux according to the criteria of the Lyon Consensus are evaluated. All the studies were performed with a Digitrapper pH-Z recorder (MEDTRONICS) and Accuvue pH-Z 5.2 software, modifying in the analysis a single element, the duration of the reflux episode.

Results: Control group of 10 subjects (mean age 22.6 ± 1.2 a.). Patients group (mean age 53.6 ± 12.2 a.). The increase in the minimum time to consider an episode of reflux was associated with a decrease in the number of episodes, of the AET and of the GS, both in the controls and in patients with reflux and the total group (TABLES WOULD BE PROVIDED).

Conclusion: Reducing the minimum time to consider a reflux episode to 2 seconds produces a significant increase in the number of episodes, with a wide standard deviation; which may affect the results of the parameters that relate reflux and symptoms (symptomatic sensitivity index, probability of symptomatic association) and the so-called undetermined group of the Lyon criteria, 10% of which would change diagnosis with criteria of minimum duration 2 or 4 seconds, a percentage that doubles when comparing 2 with 6 seconds.

Disclosure: Nothing to disclose

P0107

MEAN NOCTURNAL BASELINE IMPEDANCE CORRELATES WITH REFLUX DISEASE SEVERITY AND SYMPTOM PERCEPTION

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Introduction: The Lyon Consensus 2018 describes nocturnal baseline impedance (MNBI) as a reflection of oesophageal mucosa permeability, with lower values found in erosive and eosinophilic oesophagitis¹; however it is not clear how MNBI correlates with symptoms. This study aims to determine the relationship of MNBI with symptoms across three common presentations of reflux; Barrett's oesophagus, non-erosive reflux disease (NERD) and functional heartburn (FH).

Aims & Methods: Between 2014 and 2020, pH-Impedance measurements and symptom index (SI) were collected for 37 consecutive patients with at least 3 cm of Barrett's oesophagus. Results were compared with 37 consecutive patients with NERD and 37 with FH were used as disease controls. MNBI was calculated from sensors at 3 and 5cm above the LOS over 3x10 minute intervals during the nocturnal period.

Results: There was no significant difference between Barrett's and NERD in median acid exposure time (AET) [Barrett's 14.0% (6.3%-23.5%) vs. NERD 8.9%(5.6%-13.5%) (p=0.497)], total number of impedance-measured reflux events [Barrett's (108.5±79.8) vs. NERD (87±52.2) (P=0.444)] or bolus exposure time (BET) [Barrett's (2.49±3.2) vs. NERD (1.29±0.9) (p=0.096)]. By definition, AET 1.9(0.7%-2.7%), number of reflux events (41.24±23.5) and BET (0.48±0.3) were all within normal limits for FH.

Barrett's patients reported the fewest symptoms overall (7.5; 0-24), whereas NERD (15; 6-41) and FH (13.5; 6-28) reported a similarly increased number of symptoms. On the other hand, NERD patients were more likely to have a positive SI (12/37; 32.4%) compared to Barrett's (7/37; 18.9%) (p=0.048). Similarly, the median SI for NERD was highest (32.3%; 6.4-54.5%) compared to Barrett's (6.25%; 0-38%) (p<0.008). FH, by definition, had a negative SI (0%; 0%-8.2%).

MNBI was lowest in Barrett's compared to NERD and FH (p<0.0001) (Figure 1) There was no difference in MNBI between the 10 patients with persistent (>3cm) Barrett's who had attempts at therapy (ablation, mucosal resection) compared to the 27 who had not received therapy (p=0.96). There was a moderately inverse correlation between median Barrett's segment length (5cm (3cm,9cm)) and MNBI (r = -0.436; p=0.038).

Conclusion: This study suggests that MNBI was able to differentiate between the 3 groups, despite the similar AET, total number of reflux events and BET seen across Barrett's and NERD patients. Furthermore, the impact of reflux disease on mucosal permeability (MNBI) appears to have an influence on symptom perception. This study also provides further validation to the Lyon consensus definition of MNBI as a measure of reflux disease severity.

	Barrett's oesophagus MNBI (ohms)	NERD MNBI (ohms)	Functional Heartburn MNBI (ohms)	P-value
IQR (25th percentile)	248	2764	3809.25	p<0.0001*
Median	398	1160	3355	p<0.0001*
IQR (75th percentile)	777	964.5	2866.5	p<0.0001*

[Median and IQR MNBI for 3 presentations of reflux]

References: 1Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. Gut 2018;67:1351-1362.

Disclosure: Nothing to disclose

P0108

EVALUATING CLINICAL FEATURES AND REFLUX SYMPTOM INDEX AS DIAGNOSTIC INDICATORS OF EXTRA-OESOPHAGEAL GASTRO-OESOPHAGEAL REFLUX DISEASE

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Introduction: There is currently no gold standard investigation for Extra-Oesophageal Gastro-Oesophageal Reflux Disease (EOGORD). Identifying this condition relies heavily on clinical diagnosis and invasive investigations such as oesophageal pH monitoring and manometry. We aim to: (1) establish clinical factors associated with pathological EOGORD; and (2) assess the accuracy of Reflux Symptom Index (RSI) questionnaire, a commonly employed tool, in detecting pathological EOGORD.

Aims & Methods: We analysed data of all patients who completed an RSI questionnaire while attending a 24-hour impedance-pH study at a major tertiary centre between January 2016 to July 2018. Pathological EOGORD was defined as those who reported extra-oesophageal symptoms (cough, burp, sour taste, globus pharyngeus), and DeMeester Score >14.72 or Symptom Index ≥50% or Symptom Association Probability ≥95%. An RSI ≥13 was taken to be indicative for clinically significant extra-oesophageal reflux symptoms.

The association between gender, hiatus hernia, and BMI with pathological EOGORD were calculated using a Chi-Squared test, while age association with EOGORD was evaluated using an independent sample t-test. Performance of RSI was assessed using sensitivity, specificity, and positive and negative predictive values. Statistical analyses were performed on SPSS version 25.

Results: 72 patients fulfilled the inclusion criteria, with 35 patients meeting our definition for pathological EOGORD. BMI ≥25 was significantly associated with an increased risk of pathological EOGORD when compared to patients with BMI <25 (66.7% vs 40.4%, $p=0.036$). Gender (Female 50.0% vs Male 47.1%, $p=0.803$), age (No EOGORD 50.5 ±16.5 vs EOGORD 50.4 ±14.6, $p=0.963$), and hiatus hernia (Present 60.0% vs Absent 51.2%, $p=0.614$) were not found to be independent predictors of pathological EOGORD.

The performance characteristics analysis of RSI in detecting pathological EOGORD showed a sensitivity of 54.3%, a specificity of 75.0%, a positive predictive value of 67.9%, and a negative predictive value of 62.8%.

		Pathological EOGORD		p-value
		Absent (n=37)	Present (n=35)	
RSI	<13	27	16	N.A.
Note: 1 patient did not complete RSI	≥13	9	19	
Gender	Male	18	16	$p=0.803$
	Female	19	19	
BMI	<25	28	19	$p=0.036$
Note: 1 patient's BMI not recorded	≥25	8	16	
Hiatal hernia	Absent	21	22	$p=0.614$
Note: unable to obtain information for 19 patients	Present	4	6	
Age	Mean (years)	50.5 (±16.5)	50.4 (±14.6)	$p=0.963$

[Table 1. Clinical characteristics of study cohort and association with Pathological EOGORD]

Conclusion: In our cohort, higher BMI (BMI≥25) is linked to a higher risk of EOGORD. We found RSI to be unreliable in predicting pathological EOGORD and is not a satisfactory replacement for established GORD assessment.

Disclosure: Nothing to disclose

P0109

ARTIFICIAL INTELLIGENCE AUTOMATES EVALUATION OF BASELINE IMPEDANCE FROM PH-IMPEDANCE STUDIES AND AUGMENTS PREDICTION OF TREATMENT OUTCOME IN GASTRO-ESOPHAGEAL REFLUX DISEASE

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Introduction: Artificial intelligence (AI) automates several gastroenterologist tasks, including interpretation of endoscopic images, but has not been evaluated for pH-impedance studies. Baseline impedance (BI) is a measure of esophageal mucosal integrity, but calculation of BI from pH-impedance studies is only possible during artifact free nocturnal periods (mean nocturnal BI, MNBI). AI has potential to streamline BI acquisition, including from upright periods of the pH-impedance tracing.

Aims & Methods: We determined feasibility of automated AI in BI extraction (AIBI), and compared AIBI with acid exposure time (AET), mean nocturnal BI (MNBI), and GERD outcome.

Raw data from pH-impedance studies were acquired from symptomatic patients studied off ($n=117$, 53.1±1.2 yr, 66%F) and on ($n=93$, 53.8±1.3 yr, 74%F) antisecretory therapy at two tertiary care centers and from an international cohort of asymptomatic volunteers ($n=115$, 29.3±0.8 yr, 47%F). Data were uploaded into dedicated prototypical AI software designed to automatically extract AIBI. Manual corroboration of 2 test studies by two investigators (BDR, CPG) demonstrated almost 90% accuracy of the program in identification of swallows, reflux episodes, and belches; these events, meal periods and artifacts were digitally discarded in calculating AIBI. Manually extracted MNBI values, corresponding total, upright and recumbent AIBI, and the upright:recumbent AIBI ratio were recorded. AIBI was separately calculated from the first 30 and 60 min of the upright and recumbent pH-impedance monitoring periods for additional analysis. AIBI values were compared to AET and MNBI in controls and GERD patients, and ≥50% symptom improvement on validated questionnaires in GERD patients.

Results: Recumbent AIBI was similar to MNBI ($p=ns$). AIBI ratio was higher when AET>6% (median 1.18, IQR 1.0-1.5), compared to < 4% (0.95, IQR 0.84-1.1), 4-6% (0.89, IQR, 0.72-0.98) and controls (0.93, IQR 0.80-1.09, $p<0.04$). While MNBI, total AIBI, and the AIBI ratio off PPI were significantly different between responders and non-responders to GERD management ($p<0.05$ for each comparison), only AIBI ratio segregated management responders from other cohorts. On ROC analysis, off therapy AIBI ratio had AUC of 0.661, comparable with AET (AUC 0.715), and better than MNBI (AUC 0.313); AIBI ratio outperformed AET when AET >6% (AUC 0.766 vs. 0.606) and 4-6% (AUC 0.563 vs. 0.516). Off therapy AIBI acquired from the

first 30 and 60 min of the recumbent pH-impedance monitoring period resembled MNBI ($p \geq 0.10$); 30 min upright AIBI was lower than overall upright AIBI ($p = 0.007$), but 60 min values were similar ($p = 0.07$). Additionally, AIBI ratio calculated from the first 30 and 60 min of the upright and recumbent periods resembled overall AIBI ratio ($p \geq 0.36$ for each comparison); however, performance characteristics in predicting symptom response were less robust (30 min AIBI ratio: AUC 0.594, 60 min AIBI ratio: AUC 0.590).

Conclusion: BI calculation can be automated using AI, and can be evaluated during both upright and recumbent periods. Novel AI metrics show potential in predicting GERD treatment outcome.

	Controls	Off PPI		On PPI	
		Response	No Response	Response	No Response
	<i>n</i> =115	<i>n</i> =57	<i>n</i> =57	<i>n</i> =39	<i>n</i> =48
Total AET (%)	0.6 (0.2-1.2)	4.5 (2.0-9.4) †*	1.9 (0.7-4.2) †	0.3 (0.0-6.9)	0.4 (0.1-1.8)
MNBI (ohms)	2497 (2170-3029)	1378 (922-2027) †*	2128 (1493-2885)	1645 (1015-2571) †	1968 (1165-2593) †
Total AIBI (ohms)	2398 (1985-2908)	1513 (1058-2248) †	1968 (1535-2374) †	1785 (1274-2241) †	1865 (1543-2231) †
Upright AIBI (ohms)	2329 (1938-2834)	1450 (1025-2206) †*	1828 (1423-2272) †	1656 (1239-2245) †	1826 (1528-2127) †
Recumbent AIBI (ohms)	2468 (2111-2953)	1425 (1051-2085) †*	2070 (1623-2627) †	1621 (1052-2292) †	1835 (1428-2525) †
U:R AIBI ratio	0.93 (0.80-1.09)	1.05 (0.83-1.22) †*	0.89 (0.79-1.06)	0.96 (0.87-1.24)	0.97 (0.85-1.15)

[Table. Comparison of Reflux Metrics 5 cm above LES between Controls and GERD Patients. * $p < 0.05$ compared to no response; † $p < 0.05$ compared to controls]

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P0110

REFLUX MONITORING WITH IMPEDANCE-PH-METRY: NEW SET OF NORMAL VALUES OBTAINED FROM CONSENSUS ANALYSIS OF TRACINGS FROM HEALTHY ASYMPTOMATIC SUBJECTS: A MULTICENTRE INTERNATIONAL COLLABORATIVE STUDY

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Introduction: Existing normal values for pHmetry and impedance-pH-metry have limitations, including limited sample size of normative studies from typically one or two countries, significant technical problems from inclusion of pH drops due to meals/artefacts, and identification of impedance reflux events using inconsistent rules, leading to large inter-reviewer variability. Software for automated analysis also has significant limitations, resulting in over-diagnosis of particularly non-acidic reflux.

Aims & Methods: We aimed to obtain a new set of normal values for im-

pedance-pH-metry based on consensus analysis of tracings from a large number of healthy asymptomatic subjects collected from multiple countries in five continents.

Methods: A total of 541 Impedance-pHmetry tracings from healthy asymptomatic subjects from Africa, Asia, Europe, North America, and South America were collected and de-identified. Included studies were performed with two different systems: Diversatek (Boulder, Colorado, US) (ex Sandhill) and Medical Measurement Systems (MMS, Enchede, Netherlands). Tracings with technical artefacts, marked esophageal symptoms and features of behavioural disorders (aerophagia, supragastric belching and rumination) were excluded. The included tracings were manually analysed by two expert reviewers working together either in-person or through video-conference. Analysis included 1) editing of pH drops (to exclude artefacts and meal/drink induced pH drops), 2) recognition of impedance reflux events using strict pre-established criteria, 3) Measurement of distal mean nocturnal baseline impedance (MNBI). 4) Identification and scoring of post reflux swallow-induced peristaltic waves (PSPW).

Results: After exclusions, consensus analysis was performed in 391 tracings (Diversatek $n = 265$, MMS $n = 126$), mean age 32.7 yrs (range 18-71), 212 females/179 males. Males had more acid exposure, reflux episodes and lower MNBI at 3 cm above the LES. Subjects older than 40 yrs had lower MNBI in distal esophagus. Normal values for Diversatek and MMS systems are displayed in the table. Comparing normal values between Western countries, Asia, South America and South Africa (using identical impedance-pH-metry systems) we observed significant regional differences 1. using Diversatek, higher PSPW scores in Western countries, and higher MNBI in Asia; 2. using MMS, higher acid exposure in the Netherlands, higher MNBI in Asia and South Africa, and low MNBI in Turkey. Comparison between systems in similar world regions showed that MMS measures higher MNBI both in Western countries and Asia.

Conclusion: We established normal values for impedance pH-metry based on a large number of tracings from healthy asymptomatic subjects that could be used worldwide, obtained using manual consensus analysis and consistent criteria for inclusion of pH drops, reflux recognition, MNBI and PSPW. We identified both regional and system related differences, indicating that clinical impedance-pH interpretation needs to use normal thresholds valid for the system utilized and world region. We anticipate that these normal values will contribute to development of software algorithms for more precise and clinically useful automated impedance-pH analysis.

	total acid exposure	total number of reflux	PSPW score	MNBI 5 cm above LES	MNBI 3 cm above LES
	SAN / MMS	SAN / MMS	SAN / MMS	SAN / MMS	SAN / MMS
5 percentile	0.0 / 0.0	2.0 / 2.4	15 / 19	1395 / 1794	1384 / 1542
25 percentile	0.1 / 0.3	10 / 12	34 / 35	2207 / 2410	2281 / 2334
Median	0.4 / 1.4	21 / 30	49 / 49	2630 / 3201	3001 / 3014
75 percentile	1.2 / 2.5	34 / 43	60 / 60	3179 / 4397	2623 / 4098
95 percentile	2.8 / 5.0	55 / 78	80 / 78	3944 / 5768	4510 / 5586
	p < 0.001	p < 0.02	ns	p < 0.001	ns

[Table. Normal values of impedance-pHmetry obtained with Diversatek (ex Sandhill) and MMS systems]

Disclosure: This study was performed without financial support from companies producing impedance-pHmetry systems

P0111 WITHDRAWN**P0112** WITHDRAWN**P0113**

DEFINING REFERENCE RANGES FOR PROLONGED (96-HOUR) WIRELESS PH MONITORING USING HEALTHY CONTROLS AND PATIENTS WITH EROSIIVE ESOPHAGITIS: VALIDATION OF THE LYON CLASSIFICATION FOR GERD DIAGNOSIS

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Introduction: Technology now allows up to 96-hr wireless pH-recording in clinical practice. This is desirable because there is high day-to-day variability in esophageal pH-measurements, and it has been shown that prolonged pH-studies increase the diagnostic yield and reproducibility of gastro-esophageal reflux disease (GERD) diagnoses (Scarpulla AJG 2007). However, reference ranges and diagnostic thresholds for this methodology have not been established.

Aims & Methods: This study analysed prolonged esophageal pH recordings from healthy controls (HC) and patients with objective, endoscopic evidence of GERD. Results were used to validate the recently published Lyon Consensus Classification for GERD Diagnosis (Gyawali Gut 2018). HC underwent prolonged, wireless pH studies (Bravo™, Medtronic) at two tertiary centres. Bravo™ was inserted under sedation at endoscopy. Median and 95th percentile values were calculated for acid exposure time (AET) over 24, 48, 72 and 96-hr and compared against the "worst 24-hrs" (most pathological day). Retrospectively, the same analysis was applied to results from consecutive patients with erosive esophagitis that completed 96-hr wireless pH studies off acid suppressants for >1 week, categorized by the Los Angeles (LA) classification. Linear regression and receiver operating curve (ROC) analysis were performed with the area under the ROC curve (AUC) and Youden's index to define optimal diagnostic cut-offs.

Results: 62 asymptomatic HC were studied, of whom 40 (age 28±9 years, 72% F) completed 96-hr pH recording. Median AET was 1.4% (upper 95th percentile 4.8%) for any study day and 2.6% (7.4%) for the worst day. 136 patients with reflux esophagitis completed the 96-hr study (61 LA A, 60 B, 15 C-D). Results are summarized in table 1.

Linear regression analysis revealed a correlation between endoscopic findings, average AET ($p < 0.0001$, $R^2 = 41.7\%$) and worst day AET ($p < 0.0001$, $R^2 = 33\%$) after adjusting for gender and age. ROC analysis for the average AET differentiated the group with definite, endoscopic evidence of GERD (LA B, C, D) from HC (sensitivity 87%, specificity 93%, positive predictive value (PPV) 90%, negative predictive value (NPV) 91% for a cut-off AET of 4.4%; AUC 0.94). Similar results were present for the "worst 24-hrs" analysis (sensitivity 86%, specificity 95%, PPV 93%, NPV 90% for a cut-off AET of 7.0%; AUC 0.94).

Conclusion: This study defines the reference ("normal") range for prolonged, 96-hr ambulatory wireless pH monitoring. Additionally, pathological thresholds were identified that accurately discriminate between HC and patients with conclusive GERD diagnosis, based on the presence of erosive esophagitis. The findings provide conditional support for diagnostic criteria proposed by the Lyon Consensus, specifically that AET < 4% refutes and AET > 6% supports GERD diagnosis. By comparison, ROC

analysis based on the data presented indicates that the optimal diagnostic threshold that discriminates between HC and patients with reflux esophagitis (LA B, C, D) was 4.4% based on average AET and 7.0% based on worst day AET.

Disclosure: Nothing to disclose

	96 h Average Day	96 h Worst Day
Healthy Controls (n)	40	40
Median % AET (95th Percentile range)	1.40 (0.11-4.84)	2.60 (0.41-7.47)
Reflux Esophagitis		
LA A (n)	61	61
Median % AET (95th Percentile range)	6.10 (0.80-15.50)	9.80 (1.14-23.56)
LA B (n)	60	60
Median % AET (95th Percentile range)	8.23 (1.61-18.41)	11.65 (2.31-28.37)
LA C-D (n)	15	15
Median % AET (95th Percentile range)	9.95 (4.07-24.90)	13.50 (7.30-33.50)

[Table 1. Acid Exposure Time (AET) in healthy controls and patients with erosive reflux esophagitis]

P0114

ANALYSIS OF IONS AND ORGANIC ACIDS IN SALIVA IN DIAGNOSTICS OF GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Gastroesophageal reflux disease (GERD) is a disease caused by backflow of gastric contents into the esophagus due to the failure of physiological antireflux mechanisms and can lead to esophageal and extraesophageal symptomatology. At the current time, the gold standard in diagnostics of GERD is 24-hour multichannel intraluminal impedance and pH monitoring (MII-pH) that is invasive, time consuming and expensive diagnostic method with not clear relevance in diagnostics of extraesophageal reflux (EER) and there is a need for new faster, cheaper and more sensitive diagnostic method for detection of EER.

New potential target in diagnostic of GERD is saliva. One of the saliva's protective mechanism during a reflux episode is neutralization of gastric acid by various buffering systems. Bicarbonate and phosphate constitute major salivary buffering components. Since reflux episodes occur more frequently and have a longer duration in patients having GERD, our study investigates the hypothesis that bicarbonate and phosphate ions might be elevated in saliva.

Aims & Methods: In this work, we developed a new method for the analysis of saliva samples. We analyzed two major salivary buffering compounds bicarbonate and phosphate and seven additional anions including chloride, nitrite, nitrate, sulfate, thiocyanate, acetate and butyrate using an in-house built capillary electrophoresis instrument with capacitively coupled contactless conductivity detector (CE-C²D). The developed method was used to compare the levels of these compounds in saliva samples from 12 healthy controls and 20 patients with GERD to investigate the applicability of saliva in diagnostics of GERD.

Results: We found that chloride, phosphate, bicarbonate, and acetate were the major ions with mean concentrations in saliva of 20.1, 6.4, 5.7, and 4.6 mM, respectively. Concentrations of nitrite, nitrate, sulfate, and butyrate were lower than 1 mM.

We found that there was no significant difference in phosphate concentration between healthy and GERD patients (mean values of 6.4 and 5.7 mM, $p = 0.272$). On the other hand, there was a statistically significant difference in bicarbonate concentration. The mean bicarbonate concentration was significantly higher in saliva from GERD patients than in healthy controls (i.e. 8.1 and 5.7 mM, respectively, $p = 0.004$), confirming the initial hypothesis that the buffering ions in saliva might be elevated in GERD patients due to the need for more buffering action due to the more frequent and more prolonged reflux episodes.

Concerning all other studied analytes in saliva, there was significant difference only in nitrite concentration between the two studied groups. However, it must be noted that in many cases, the nitrite levels were below LOD that could have influenced the statistical analysis.

Conclusion: In this work, we first optimized a separation electrolyte for sensitive analysis of phosphate, bicarbonate, and other inorganic and organic ions by CE-C⁴D. In total, nine ions were analyzed in saliva samples from healthy volunteers and patients suffering from GERD. Statistically significantly elevated bicarbonate levels were found in the group of GERD patients, confirming our hypothesis that natural saliva buffering compounds might be elevated in patients due to recurrent acid reflux episodes. The developed CE-C⁴D method might be useful in a non-invasive diagnostics of GERD and might contribute to a simplification of the diagnostic procedure.

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P0115

THE INFLUENCE OF CRURAL DIAPHRAGM ON ESOPHAGOGASTRIC JUNCTION FUNCTION AND GASTROESOPHAGEAL REFLUX DISEASE FEATURES. A PROSPECTIVE STUDY WITH HIGH RESOLUTION MANOMETRY AND IMPEDANCE-PH MONITORING

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Introduction: A normal esophagogastric junction (EGJ) is essential in preventing gastroesophageal reflux disease (GERD). Crural diaphragm (CD) is responsible for a part of the antireflux barrier. High-resolution manometry (HRM) provides information on axial separation between LES and CD (e.g. hiatal hernia, HH) and can evaluate the EGJ antireflux barrier thanks to the esophagogastric contractile integral (EGJ-CI). However, comprehensive

data about the correlation between presence of LES-CD separation, EGJ-CI and GERD features, such as symptoms, esophagitis and reflux patterns determined at impedance-pH monitoring (MII-pH) are scarce.

Aims & Methods: To verify if a increasing distance of LES-CD separation and a decreasing EGJ-CI could better correlate with a positive MII-pH, with reflux symptoms and with different grades of esophagitis. Secondary aim point was to verify the usefulness of a new metric to determine the CD's barrier function.

Consecutive patients with typical GERD symptoms (heartburn and/or regurgitation) and a recent upper endoscopy were enrolled. Esophagitis was defined according to Los Angeles classification. The presence of further symptoms and PPIs response were recorded. All patients underwent HRM assessing EGJ morphology, EGJ-CI, esophageal peristalsis and EGJ function. EGJ Type I was further divided into Type I-CO, a complete overlap of LES and CD, and Type I-MS, a minimal separation, with LES located from the upper border of CD (in correspondence of pressure inversion point, 0.0 cm) to 1 cm above. Also, intra-hernia pressure and contractile integral of CD (CD-CI, using a DCI toolbox for three respiratory cycles and then dividing for the duration in seconds, when distinguishable from LES, e.g. not in Type I-CO) were recorded.

The patients then underwent impedance-pH testing off-therapy. We recorded the esophageal acid exposure time (AET), number of total impedance-detected reflux episodes, mean nocturnal baseline impedance (MNBI), post-reflux swallow-induced peristaltic wave index (PSPW, + if < 53%) and symptom association analysis using symptom association probability (SAP+ if $\geq 95\%$) and symptom index (SI+ if $\geq 50\%$).

McNemar test and Anova test were performed among the four group determined according to LES-CD separation.

Results: We enrolled 203 [96M/107F; mean age 46 (17-82)] consecutive patients and identified 72 (35.4%) EGJ Type I-CO, 54 (26.6%) Type I-MS, 42 (20.7%) Type II and 35 (17.2%) Type III. Patients with Type III EGJ had lower EGJ-CI, decreased mean DCI, a higher median number of reflux episodes, a greater mean AET, a lower MNBI and PSPW and had more frequently a positive symptoms association compared to patients with Type II and Type I-CO/MS (Table 1). Type I-MS had a higher number of reflux episodes (48 vs. 29, $p < 0.03$), a greater mean AET (4.8 vs. 2.7, $p < 0.05$) and a greater positive symptom association (55% vs. 26%, $p < 0.02$) compared to Type I-CO. A low value of CD-CI was present in 55% of HH and the lower the values, greater were the number of refluxes or AET values. At Anova, PPI response was significantly linked to EGJ Type III, whereas dysphagia presence was linked to higher intra-hernia pressure and higher CD-CI values.

Conclusion: With increasing separation between the LES and the CD patients had a gradually and significantly increase of reflux episodes and esophageal acid exposure. Even a minimal separation can be responsible for GERD development and supports the role of the CD in preventing reflux. Assessing contractility integral for CD could be important for evaluating both presence of severe GERD (when low) and dysphagia (when high).

Disclosure: Nothing to disclose

P0116

OGJ-CI COMPLEMENTS REFLUX DISEASE SEVERITY AND GIVES INSIGHT INTO THE PATHOPHYSIOLOGY OF REFLUX IN BARRETT'S

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Introduction: Oesophagogastric junction contractile integral (OGJ-CI) is a novel parameter that assesses barrier function during high resolution manometry (HRM); however its utility has not yet come into routine clinical

cal use. We assessed OGJ-CI values across three common presentations of reflux; Barrett's oesophagus, non-erosive reflux disease (NERD) and functional heartburn (FH), to determine how OGJ-CI complements disease severity. Analysis was replicated across 2 common HRM systems and catheter types in consecutive patients.

Aims & Methods: Consecutive HRM studies between 2014 and 2020 were collected from a tertiary referral unit in London; 63 patients (21 Barrett's, NERD and FH each) used a water-perfused catheter (Medical Measurement System, Netherlands) and 48 patients (16 Barrett's, NERD and FH each) used a solid state catheter (Sierra Scientific Instruments, USA). OGJ-CI was calculated using the distal contractile integral (DCI) tool over 3 respiration cycles at 20mmHg isobaric contour. DCI of the oesophageal body was used as a measure of peristaltic effectiveness. Manometry was followed by 24 hour catheter-based pH monitoring to measure acid exposure time (AET) and is presented as (median; interquartile range).

Results: Overall, AET was greatest in patients with Barrett's (14%; 5.8-23.6%) followed by NERD (9.3%; 5.8-13.6%) and FH (1.9%; 0.8-2.8%) ($p < 0.0001$). Similar OGJ-CI and DCI pressure trends were seen across both manometry systems and catheter types. There was no statistical difference in OGJ-CI between NERD and FH (Sierra $p=0.9$; MMS $p=0.614$) but OGJ-CI was significantly lower in patients with Barrett's compared to NERD and FH (Sierra: $p=0.014$; MMS: $p=0.017$) (Figure 1). Similarly, DCI was higher in NERD (Sierra 659mmHg.s.cm; MMS 588mmHg.s.cm) and FH (Sierra 1202mmHg.s.cm; MMS 736mmHg.s.cm) while in Barrett's, DCI was significantly lower (Sierra 417mmHg.s.cm; MMS 198mmHg.s.cm) (Sierra $p=0.002$; MMS $p < 0.0001$). A weak negative correlation was observed between Barrett's length and OGJ-CI ($r=-0.18$, $p=0.5$).

	MMS Barrett's oesophagus OGJ-CI (mmHg.cm)	MMS NERD OGJ-CI (mmHg.cm)	MMS Functional Heartburn OGJ-CI (mmHg.cm)	Sierra Barrett's oesophagus OGJ-CI (mmHg.cm)	Sierra NERD OGJ-CI (mmHg.cm)	Sierra FH OGJ-CI (mmHg.cm)
95% CI (Upper limit)	17.9	39.6	37.0	7.6	40.0	31.7
Median	13.0	29.1	27.1	4.2	24.0	19.8
95% CI (Lower limit)	8.0	18.7	17.3	0.8	8.0	7.9

[Median OGJ-CI (mmHg.cm) with 95% Confidence Interval (CI) across 3 presentations of reflux, using MMS and Sierra]

Conclusion: OGJ integrity and peristaltic effectiveness correlate well with acid reflux burden but the mechanism differs between reflux disease states; OGJ-CI is the same between NERD and FH but markedly reduced in Barrett's. Further, DCI is higher in NERD and FH than in Barrett's. Furthermore, this pattern is similar across two of the most commonly used HRM systems and are independent of catheter characteristics. This study suggests that in Barrett's, disruption of OGJ anatomy may result in an increased volume of reflux compounded by reduced peristalsis effectiveness (and in turn, clearance), whereas in NERD, the increased frequency of reflux is more likely to be cleared by an intact peristaltic contraction.

Disclosure: Nothing to disclose

P0117

MEAN NOCTURNAL BASELINE IMPEDANCE VALUES DO NOT CORRELATE WITH SYMPTOMS AND SIGNS OF LARYNGOPHARYNGEAL REFLUX AND DO NOT PREDICT RESPONSE TO PPI THERAPY

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Introduction: 24 hour pH impedance has been increasingly used for the diagnosis of laryngopharyngeal reflux (LPR). However, no criteria for the pathologic number of LPR episodes have been widely accepted yet. Therefore reflux symptom index (RSI), reflux finding score (RFS) and therapeutic PPI trial have remained the gold standard of diagnosis and treatment. Recently, mean nocturnal baseline impedance (MNBI) gained substantial evidence for the diagnosis of GERD. Nevertheless, the evidence of MNBI for its use in LPR patients is scarce. We therefore formulated the hypothesis that lower MNBI values are associated with higher symptom burden, more severe reflux laryngitis and predict response to PPI therapy in patients with LPR.

Aims & Methods: Patients referred for suspected LPR were screened and those with positive reflux finding score (RFS>7), as determined by flexible laryngoscopy and/or positive reflux symptom index (RSI>13), and at least one acidic LPR episode during 24 hour pH/impedance study were enrolled. We recruited patients at least 30 days without PPI treatment. Appropriate distance between pH sensors was chosen based on manometrically determined upper and lower esophageal sphincter. We reviewed the pH impedance tracings and determined MNBI values as the average value of three 10 min. intervals (1:00, 2:00 and 3:00 a.m.) in the periods without reflux events and/or swallowing. We gained these values for 6 impedance segments (Z1 - most proximal to Z6 - most distal). We established the correlation between the MNBI values and RSI/RFS using Pearson correlation coefficient (R value). Then we recommended PPI treatment twice daily for 3 months. Subsequently we determined RSI values and evaluated symptomatic response. We determined those who achieved RSI normalization or > 50% decrease of RSI as PPI responders. Those that did not fulfill these criteria were the non-responders group. We compared the pre-treatment MNBI values in these groups of patients using Students T-test.

Results: 27 patients (20M/7F) completed the study. RSI in RSI positive patients 25.4[24-33.5] and RFS in RFS positive patients was 10[9-11]. Average MNBI values before PPI treatment were 2816±135Ω, 3361±162Ω, 3376±196Ω, 2490±171Ω, 2469±252Ω and 2974±320Ω for segments Z1-Z6, respectively. There was no correlation between MNBI and RSI in any impedance segment ($R=0.15$, -0.08 , -0.12 , 0.02 , 0.07 and -0.14 , for segments Z1-Z6, respectively, $p=NS$ in all cases). There was also no correlation between MNBI and RFS ($R=-0.05$, 0 , -0.09 , -0.22 , -0.26 , -0.2 for segments Z1-Z6, respectively, $p=NS$ in all cases). 18 patients completed 3 months treatment. 8 patients were PPI responders and 10 patients were PPI non-responders. There was significant increase of MNBI values in Z4-Z6 ($p < 0.04$ in all three segments), and no significant increase of MNBI in Z1-Z3 compared to pretreatment values ($N=18$). There was no statistical difference between pretreatment MNBI values in the responders compared to non-responders group in any impedance segment ($p=0.28$, 0.79 , 0.94 , 0.72 , 0.79 , 0.92 in Z1-Z6, respectively).

Conclusion: Direct relationship between the microscopic mucosal injury and the symptoms and signs of laryngopharyngeal reflux is improbable. Moreover, MNBI values do not predict symptomatic response to PPI. This suggests that other aspects of LPR than those that are detectable on 24 hour esophageal pH/impedance might be of importance.

Disclosure: Nothing to disclose

P0118

EXTRAESOPHAGEAL SYMPTOMS OF GERD: CAN MICROSCOPIC ESOPHAGITIS IMPROVE THE DIAGNOSIS?

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Introduction: Establishing causality between Gastroesophageal reflux disease (GERD) and extraesophageal symptoms is extremely challenging. Current diagnostic tests suffer from either lack of sensitivity or specificity and have limited associated treatment outcomes. Combination of different methods is often needed to support or refute this diagnosis.

Aims & Methods: We aimed to evaluate the performance of a standardized protocol to identify microscopic esophagitis and to determine its role in supporting laryngopharyngeal reflux (LPR) diagnosis related to GERD. Thus, a unicentric, observational, prospective study was performed between April and October 2019 in the Otorhinolaryngology (ORL) department of Braga Hospital, with 39 patients with suspected LPR according to clinical symptoms and signs. The Reflux Symptom Index (RSI) questionnaire and the Reflux Finding Score (RFS) on nasopharyngolaryngoscopy evaluation were obtained. Upper gastrointestinal endoscopy with microscopic esophageal evaluation as defined by the Esohisto consensus guidelines, conventional esophageal manometry and combined esophageal pH-impedance monitoring were also performed off Proton Pump Inhibitor (PPI).

Results: From the 39 suspected LPR, most patients were female (87,2%), with a mean age of 57,7 years old, with concomitant esophageal symptoms in 92,3% and only 25,6% responded to IBP treatment. The mean RSI and RFS were 23,4 and 11, respectively. GERD was confirmed in 45,7% of patients. The RSI item coughing after eating/lying down showed to be a significant predictor for GERD in patients with suspected LPR (OR:1.6; p=0.036). The total RSI score displayed an AUC of 0.696 (SE=0.09, p=0.036), with a sensitivity of 81,3% and specificity of 57,9%, when a cut-off of 20 was selected. Microscopic esophagitis revealed a sensitivity of 35,7% and specificity of 70,0% in our sample, though severe esophagitis (n=2) was only found in GERD patients.

Conclusion: The Esohisto histological score revealed a low performance to identify patients with LPR related to GERD, though it may improve upper endoscopy performance

Disclosure: Nothing to disclose

P0119 WITHDRAWN

P0120 WITHDRAWN

P0121

A CHINESE SUBGROUP ANALYSIS OF THE ASIAN PHASE 3 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF VONOPRAZAN 10 OR 20 MG COMPARED WITH LANSOPRAZOLE 15 MG IN THE MAINTENANCE TREATMENT OF ASIAN PATIENTS WITH EROSIIVE ESOPHAGITIS

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Introduction: Proton pump inhibitors (PPIs) such as lansoprazole are standard therapy for short-term and maintenance treatment of erosive esophagitis (EE). However, PPIs show variable time to onset of action and high relapse rate of healed EE. Vonoprazan, a potassium competitive acid blocker, offers maximum acid-inhibitory effects in first dose compared with lansoprazole. Previous phase III study had shown the non-inferiority of vonoprazan to lansoprazole in non-Japanese Asian EE patients during the initial therapy phase. However, whether vonoprazan was also non-inferior to lansoprazole during the maintenance phase of EE therapy in non-Japanese Asian patients was not clarified. A study was conducted to assess the safety and efficacy of vonoprazan in Non-Japanese Asian patients with healed EE. In this sub-group analysis, the non-inferiority of vonoprazan compared to lansoprazole in the maintenance phase of healed EE in Chinese patients was evaluated.

Aims & Methods: A phase III, double-blind, parallel-group, multicenter study was conducted to demonstrate the non-inferior efficacy and safety of vonoprazan to lansoprazole in non-Japanese Asian patients with healed EE (NCT02388737). Adult patients with endoscopically confirmed EE were randomized (1:1:1) to receive oral vonoprazan 10 or 20 mg once daily (QD) or lansoprazole 15 mg QD as maintenance therapy for 24 weeks. Primary end point was EE recurrence rate during the 24 weeks, which is defined as endoscopically confirmed Los Angeles classification grade A-D EE. Additional end points included subjective measures of EE symptoms, health-related quality of life (HRQoL), and safety. In this subgroup analysis, we report the efficacy and safety of vonoprazan (10 and 20 mg) compared with lansoprazole (15 mg) in Chinese patients with healed EE.

Results: In the Chinese cohort, 491 patients randomly received oral vonoprazan 10 mg (N=163) or 20 mg (N=159) QD or lansoprazole 15 mg QD (N=169) as maintenance therapy for 24 weeks. Endoscopically confirmed EE recurrence rates during 24 weeks were 13.8% (17 of 123) in the vonoprazan 10-mg group, 14.0% (17 of 121) in the vonoprazan 20-mg group, and 25.0% (31 of 124) in the lansoprazole 15-mg group. Vonoprazan 10 mg (treatment difference: -11.2%, 95% CI: -20.9, -1.4) and 20 mg (treatment difference: -11.0%, 95% CI: -20.8, -1.1) were non-inferior to lansoprazole in preventing recurrences of EE after 24 weeks. As the upper limit of 95% CIs was ≤0%, both doses of vonoprazan showed superiority to lansoprazole. EE symptoms were improved in all treatment groups from baseline, with no significant between-group difference ($P>.05$). HRQoL measures assessed using EQ-VAS scores were significantly greater in the vonoprazan 10-mg group than in the lansoprazole 15-mg group ($P=.004$). Treatment-emergent adverse event (TEAE) rates were 71.8%, 78%, and 72.2% for vonoprazan 10 mg, vonoprazan 20 mg, and lansoprazole 15 mg, respectively, out of which the incidence rates for drug-related TEAEs were 23.9%, 28.3%, and 16.6%, respectively; 4.9%, 4.4%, and 5.3% of patients in

the three groups, respectively, reported serious adverse events, although none of them were related to the study drug. Treatment discontinuation due to TEAEs was 6.1% with vonoprazan 10 mg, 5.7% with vonoprazan 20 mg, and 4.1% with lansoprazole. Upper respiratory infection was the most frequently reported TEAE in the vonoprazan 10-mg (17.2%), 20-mg (15.7%), and lansoprazole groups (11.8%).

Conclusion: Vonoprazan 10 and 20 mg are well tolerated and superior to lansoprazole 15 mg for preventing relapse in Chinese patients with healed EE.

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P0122 WITHDRAWN

P0123

UNDERSTANDING THE PPI-USER JOURNEY: RESULTS OF A SURVEY ON INITIATION OF PPI TREATMENT

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Introduction: PPIs are one of the most widely-prescribed classes of medication for the treatment of reflux¹. Under current guidance, patients with GORD or un-investigated dyspepsia should be initially offered lifestyle advice and antacid/alginate therapy². If unsuccessful, the next step is to is to offer empirical full-dose PPI therapy for 4-8 weeks². Long-term PPI use should be regularly reviewed and the lowest effective dose prescribed^{2,3}. Currently, however, physicians are inclined to prescribe a PPI early and for extended periods, which presents a barrier to appropriate reflux management¹.

Aims & Methods: The aim of this piece of research is to better understand the impact of current practice on patient attitudes and treatment journeys.

An online survey was conducted by Toluna/Harris Interactive with sufferers of gastroenterological conditions in the UK and Germany (DE) in December 2019. 6088 (UK) and 4640 (DE) respondents were screened and a total of 566 (n=372 UK; 194 DE) qualified for participation in the survey. Either a 5- or 20-minute survey was taken depending on the sample group. Respondents were included if they were either current or previous users of PPIs who: (1) Are currently using a PPI to treat reflux; (2) Have in the last year used a PPI to treat reflux; (3) Have in the last year used a PPI for another reason. Current users of PPI for any other reason were excluded. The following topics were covered (bold indicates responses from groups 1-3, otherwise only responses from groups 1&2): Steps taken before first visiting physician with reflux, Initial recommendations, PPI treatment initiation, Use of PPI, Management of reflux whilst taking a PPI, Ending PPI Treatment, Attitudes towards taking a PPI.

Study Limitations: This study explored individual recall of PPI treatment initiation and use thereafter. This methodology is appropriate as an insights tool; however, it is not a validated patient reported outcome (PRO) measure. Future research would be carried out using a validated PRO.

Results: Approximately 10% of the UK population and 5% in Germany (DE) are currently on, or recently completed, a PPI course (n=6088 UK; 4640 DE). The majority (7% UK; 3% DE) of these prescriptions were for reflux. 79% UK and 69% DE respondents reported being prescribed something at first visit; of these, 61% UK and 68% DE were prescribed a PPI either alone or in combination with another treatment. 20% of respondents (20% UK; 17% DE) reported not having tried any over-the-counter (OTC) medication prior to being prescribed a PPI. Those prescribed a PPI recalled being well informed about what dosage to take (70% UK; 69% DE) and when to take it (56% UK; 58% DE) when first prescribed a PPI; however, other safety and usage information was not as frequently discussed (Table 1).

	UK	Germany (DE)
What dosage to take each day	70	69
When to take the PPI	56	58
How long you should keep taking the PPI	22	38
What to do if you get side effects	19	18
Interactions with other medications	18	27
Side effects	18	23
How long for the PPI to take effect	17	30
Possible symptoms once stop taking PPI	15	19
Nothing	8	5

[Table 1. Information Provided Alongside PPI Prescription]

Conclusion: There is user-reported variability in treatment and prescription approach of PPIs as compared to standard guidance. Respondents recalled being commonly informed about dosing when first prescribed a PPI but other key pieces of safety and usability information were not as commonly reported as discussed.

References: 1Coyle C et al. BJGP Open, 2019 ; 2NICE Clinical guideline [CG184]; Last updated: 2019; 3 Freeberg, et al, Gastroenterology 2017;152:706-715

Disclosure: The authors are employees of Reckitt Benckiser Healthcare Ltd.

P0124

UNDERSTANDING THE PPI-USER JOURNEY: RESULTS OF A SURVEY ON PPI TREATMENT EXPERIENCE

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Introduction: PPIs are one of the most widely-prescribed classes of medication for the treatment of reflux¹. Under current guidance, patients with GORD or un-investigated dyspepsia should be initially offered lifestyle advice and antacid/alginate therapy². If unsuccessful, the next step is to is to offer empirical full-dose PPI therapy for 4-8 weeks². Long-term PPI use should be regularly reviewed and the lowest effective dose prescribed^{2,3}. Currently, however, physicians are inclined to prescribe a PPI early and for extended periods, which presents a barrier to appropriate reflux management¹.

Aims & Methods: The aim of this piece of research is to better understand the impact of current practice on patient attitudes and treatment journeys. An online survey was conducted by Toluna/Harris Interactive with sufferers of gastroenterological conditions in the UK and Germany (DE)

in December 2019. 6088 (UK) and 4640 (DE) sufferers were screened and a total of 566 respondents (372 UK; 194 DE) qualified for participation in the survey. Either a 5- or 20-minute survey was taken depending on the sample group. Respondents were included if they were either current or previous users of PPIs who: (1) Are currently using a PPI to treat reflux; (2) Have in the last year used a PPI to treat reflux; (3) Have in the last year used a PPI for another reason. Current users of PPI for any other reason were excluded. The following topics were covered (bold indicates responses from groups 1-3, otherwise only responses from groups 1&2): Steps taken before first visiting physician with reflux, Initial recommendations, PPI treatment initiation, Use of PPI, Management of reflux whilst taking a PPI, Ending PPI Treatment, Attitudes towards taking a PPI.

Study Limitations: This study explored individual recall of PPI experience on initiation and use thereafter. This methodology is appropriate as an insights tool; however, it is not a validated patient reported outcome (PRO) measure. Future research would be carried out using a validated PRO.

Results: Most respondents reported taking their PPI for more than 2 months; up to two thirds have been taking PPIs continuously for over 1 year (64% UK rising to 78% aged 55+, 50% DE rising to 62% aged 55+). 1 in 3 (33% UK;29% DE) reported taking their PPI for 5 years or more (Table 1). 88% of UK and 80% of DE respondents prescribed PPIs either do not know how long they will be taking a PPI for (41% UK;48% DE) or expect to be taking their PPI for over 3 months (47% UK;32% DE). The majority of PPI users reported experiencing breakthrough symptoms (66% UK;80%DE). For half of this group, symptoms occurred once a week or more (47% UK;48% DE). In both countries, of those who had come off their PPI, half abruptly stopped treatment (49%UK;56%DE); the other half either reduced dose or frequency (51% UK;44% DE).

Reported Duration of PPI Use	UK (%)	Germany (DE) (%)
Longer than 5 years	33	29
3-5 years	16	13
1-2 years	16	8
7-12 months	5	8
3-6 months	8	10
1-2 months	6	9
2-4 weeks	9	14
1 week	4	5
Cannot remember	4	5

[Table 1. Reported duration of PPI use (numbers rounded)]

Conclusion:

- Over two thirds of respondents experienced breakthrough symptoms, half of these at least once a week.
- PPI treatment duration exceeded guideline limits in most cases.
- Half of PPI users who stopped their PPI reported doing so abruptly.

References: References: 1Coyle C et al. BJGP Open, 2019, 2NICE Clinical guideline [CG184]; Last updated: 2019, 3 Freeberg, et al, Gastroenterology 2017;152:706-715

Disclosure: The authors are employees of Reckitt Benckiser Healthcare Ltd.

P0125 WITHDRAWN

P0126 WITHDRAWN

P0127 WITHDRAWN

P0128 WITHDRAWN

P0129

REAL WORLD RISK OF ACUTE INTERSTITIAL NEPHRITIS IN PATIENTS ON ACUTE PROTON PUMP INHIBITOR THERAPY

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Introduction: Proton pump inhibitors (PPIs) are one of the most commonly prescribed medications for management of many gastrointestinal disorders, including gastroesophageal reflux disease, peptic ulcer disease, dyspepsia, Barrett's esophagus, and acute gastrointestinal bleeding. PPI are generally well tolerated and are thought to have a good safety profile. However, studies suggest a link between chronic PPI and renal dysfunction, specifically acute interstitial nephritis (AIN). Diagnosis is usually delayed due to its atypical and subtle presentation, which likely contributes to its progression to chronic kidney disease (CKD). There is limited data on whether acute PPI therapy causes AIN. Our primary aim was to evaluate the prevalence of AIN in patients for each acute PPI therapy medication. Our secondary aim was to compare the risk of AIN in patients on PPI compared to histamine H2-receptor blockers (H2 blockers) and compare adverse outcomes of acute PPI-induced AIN.

Aims & Methods: We performed a retrospective analysis in the IBM Explorys database 5 (1999-2020), a pooled, national, de-identified clinical database of over 72 million unique patients from 26 health care networks and 300 hospitals across the United States. Patient populations were identified using SNOMED and ICD codes. PPI included were esomeprazole, omeprazole, pantoprazole and lansoprazole. The development of AIN was evaluated within 8 weeks of PPI initiation. Patients on medications commonly implicated in AIN which included non-steroidal anti-inflammatory drugs, antibiotics, loops diuretic, H2 blockers, rifampin, and allopurinol were excluded from the study if prescribed within 30 days of initiation of PPI. Additionally, patients with systemic lupus erythematosus, sarcoidosis, Granulomatosis with polyangiitis, and Sjogren's disease were also excluded from the study. The control group was defined as patients on H2 blockers with the above exclusion criteria. Adverse events (AEs) were defined as ICU admission within 7 days, hemodialysis within 2 weeks, new chronic kidney disease within 6 months of diagnosis of AIN, and new end stage renal disease within 1 year for PPI group and control group. Prevalence was reported for each PPI. Odds ratio with 95% CI were calculated for risk of AIN for each PPI compared to control group. Chi-squared test was used to compare the risk of AEs in the combined PPI group vs H2 blockers.

Results: Acute PPI-induced AIN comprised 0.56% (n=1410) of total AIN patients. Prevalence of AIN in Esomeprazole was 6 (per 10,000), Omeprazole was 6 (per 10,000), Pantoprazole was 18 (per 10,000) and Lansoprazole was 4 (per 10,000). Pantoprazole was the only PPI associated with an increased risk for AIN (OR 1.66, 95% CI 1.51-1.84) compared to the control group. There was no difference between risk of CKD and ESRD between PPI and H2 blocker groups. Patients in PPI group were more likely to be senior (age > 65), female gender, have Medicare insurance, hypertension, hyperlipidemia and heart failure.

Conclusion: Our study shows that AIN is a rare side effect of acute PPI therapy. Pantoprazole should be used with caution perhaps in patients with underlying CKD however this needs to be validated in future studies.

Demographics	PPI (n=1410)	H2 blocker (n=770)	p value
Age > 65	590 (42%)	250 (33%)	<0.0001
Female	1210 (86%)	630 (82%)	0.013
Caucasian	1070 (76%)	570 (74%)	0.3
Obesity	650 (46%)	340 (44%)	0.37
Hypertension	1090 (77%)	540 (70%)	0.0003
Diabetes Mellitus	610 (43%)	310 (40%)	0.17
Heart failure	510 (36%)	210 (28%)	0.0002

[Table. Demographics of patient on PPI and H2 blockers]

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Disclosure: Nothing to disclose

P0130

PREVENTION OF ESOPHAGEAL STRICTURE AFTER CIRCUMFERENTIAL ENDOSCOPIC SUB-MUCOSAL DISSECTION: EFFECT OF A SELF-ASSEMBLED PEPTIDE IN A SWINE MODEL

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Introduction: Circumferential *en bloc* resection of esophageal mucosa using endoscopic sub-mucosal dissection (ESD) or endoscopic mucosal resection (EMR) could find its place in the treatment of Barrett's esophagus (BE) or extensive superficial neoplasia.

However, expansion of this treatment could be limited by the high risk of occurrence of an esophageal stricture. When resection exceed ¾ of the circumference, the risk to develop a stricture rise to 90%. *En bloc* circumferential esophageal mucosa resection technique have been developed in a swine model.

The aim of this study was to assess the effect of a modified, pH = 2, self-assembled peptide matrix (4[Arg-Ala-Asp-Ala]) (SAP) on the development of esophageal stricture after circumferential endoscopic resection in a swine model.

Aims & Methods: We realized an endoscopic circumferential endoscopic sub-mucosal dissection (c-ESD) in 35 swine under general anaesthesia. Five animals were included in the control group, 11 animals received the SAP matrix immediately after a c-ESD and 11 received the SAP matrix associated to a local steroid (triamcinolone 10 mg/mL) immediately after the c-ESD. An endoscopy and an esophagogram were realized at day 14 and then the animals were euthanized. Partial *en bloc* esophagectomy was realized for pathology analysis. Four animals in the SAP matrix-steroid group and 11 animals in the SAP matrix alone group were kept alive until day 28 or euthanized before this date if they developed a symptomatic

stricture. A blood sample was taken for all animals at day 0 and 14 and pro fibrotic cytokine level was determined. Our primary outcome was occurrence of an esophageal stenosis at day 14.

Results: At day 14, all animals in the control group, 10 animals in the SAPM-group (66%) and 11 (78%) animals in the SAPM-triamcinolone group had an endoscopic stricture which was symptomatic for 5 (100%), 4 (27%) and 7 (50%) of them respectively (p=0.008 for control vs SAP group, p=0.11 for control vs SAP-triamcinolone group).

Median (IQR) esophageal diameters were 8 (4.5-9.5) mm, 4.8 (3.1 - 7.7) mm and 3 (2-4) mm in the SAP, control and SAP-triamcinolone groups, respectively (p = 0.02 for control vs SAP group, p=0.11 for control vs SAP-triamcinolone group).

Concerning histological analysis, neopithelium was longer in both treated groups than in control group (p=NS). There was no correlation between TGF-β blood levels and occurring of stenosis or fibrosis depth measured on histological slides of the esophageal tissue.

Conclusion: Application of a SAP matrix upon an endoscopic esophageal c-ESD in a swine model immediately at the end of procedure allowed a 73% significant reduction of the incidence of a symptomatic stricture at day 14, by delaying its occurrence. Adding triamcinolone brought no significant improvement.

Disclosure: The study was funded by 3-D Matrix Europe SAS.

P0131

CONTRIBUTION OF HYDROGEN SULFIDE-PRODUCING CYSTATHIONINE-G-LYASE (CTH) IN THE DEVELOPMENT OF BARRETT'S METAPLASIA-SPECIFIC MOLECULAR PROFILE AND SYSTEMIC INFLAMMATION

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Introduction: Barrett's Esophagus (BE) is a premalignant condition of esophageal epithelium with characteristic molecular profile related to the expression of columnar epithelium-specific genes with special emphasis on *KRT* family. On the other hand, hydrogen sulfide (H₂S) releasing pharmacological tools have been shown to accelerate ulcer healing and to prevent gastric mucosa against NSAIDs-induced injury. H₂S is an endogenous gaseous molecule produced *via* L-cysteine metabolism due to activity of cystathionine-g-lyase (CTH) and two other enzymes. However, the involvement of H₂S-producing CTH activity in the development of BE-like molecular profile in esophageal epithelium has not been investigated.

Aims & Methods:

In vitro studies:

Human-derived esophageal keratinocytes (EPC2) and squamous esophageal epithelial cells (Het-1A) with or without CTH gene knock-outs (k/o) induced by CRISPR/Cas9 were treated with acidified bile mixture (BM) to induce BE-like molecular profile according to our previously optimized protocol reflecting clinically observed alterations. Additionally, wild type Het-1A and EPC2 cells were treated with D,L-propargylglycine (PAG, 50-1000 mM) as CTH inhibitor. BE-like molecular profile interpreted as alterations in mRNA expression of *KRT* genes (e.g. *KRT4*, *KRT8*, *KRT15*, *KRT18*) was assessed by real-time PCR. Cell viability after 3-days of treatment with PAG (50 μM-10 mM) was evaluated by thiazolyl blue tetrazolium bromide (MTT) assay.

In vivo studies:

Wistar rats with surgically-generated esophagogastrroduodenal anastomosis (EGDA) were treated i.g. for 8 weeks with vehicle or with PAG (1-30 mg/kg). Esophageal lesions/metaplasia index (ELMI) was assessed macroscopically and microscopically using H&E and PAS staining and standardized scale. Esophageal blood flow (EBF) was measured by laser flowmetry. Esophageal mRNA expression for BE-specific *KRT* genes was determined by real-time PCR. H_2S production by CTH activity in esophageal mucosa was assessed using methylene blue method. Serum content of IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-10, IL-12, TNF- α , IFN- γ , and GM-CSF was screened by Luminex platform.

Results:

In *in vitro* cell model, PAG treatment (50-1000 μ M) and CTH k/o did not affect Het-1A and EPC2 cell viability. Moreover, BM treatment of cells without genetic modifications administered with PAG, as well as Het-1A and EPC2 with CTH k/o further enhanced molecular changes characteristic for BE (e.g. *KRT* genes up/downregulation), previously observed in BM-treated EPC2 and Het-1A wild type cells.

In animal model, daily treatment with PAG (as compared with vehicle) increased ELMI evoked by chronic reflux leading to BE-like metaplasia with the presence of goblet cells, decreased EBF and induced BE-like molecular profile. Further enhancement of decreased H_2S production was observed in esophageal mucosa of EGDA-rats treated with PAG. Pharmacological inhibition of CTH by PAG increased pro-inflammatory markers serum concentration.

Conclusion: We conclude that altered H_2S production by decreased enzymatic CTH activity in esophageal mucosa exposed to gastroesophageal reflux could be involved in the development of BE metaplasia followed by specific molecular profile changes. Pharmacological inhibition of CTH and/or CTH k/o further enhanced BE progression and inflammatory response in animal model and molecular profile alterations towards BE in human esophageal epithelial cells *in vitro*, respectively. These effects possibly involve vasodilatory and anti-inflammatory properties of endogenous H_2S . [Funding source: National Science Centre, Poland (UMO-2016/23/D/NZ4/01913)].

Disclosure: Nothing to disclose

P0132

MIRNA BIOMARKERS FOR A NON-INVASIVE DIAGNOSIS OF BARRETT'S ESOPHAGUS

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Introduction: In developed countries, esophageal adenocarcinoma (EAC) incidence has increased six-fold in the last three decades. The outcome remains poor with a 5-year survival of under 20%. EAC can be preceded by Barrett's esophagus (BE). Screening the population at risk for BE would improve their surveillance schemes and help identify where early endoscopic intervention is required. To date screening has not been recommended due to reliance on expensive and invasive endoscopy. The Cytosponge® is a minimally invasive, non-endoscopic cell sampling device for BE. Cytosponge is a capsule on a string that when swallowed dissolves to an expandable sponge which can sample cells from the entire oesophageal length. The presence of gastric cardia (GC) glands in the sponge is a quality control for distal esophagus sampling and a Cytosponge is classed as inadequate if it does not include GC. A fluid-based assay, such

as miRNA applied to harvested cells could allow for greater multiplexing. We hypothesised that the combination of miRNAs with computer vision techniques could enable the determination of cell specific contributions to biomarker expression.

Aims & Methods: Cytosponge samples from the BEST2 trial were used.

i) RNA extracted from FFPE sections was probed with a custom 110-plex miRNA panel (Fireplex, Abcam) containing known and novel biomarker candidates. Cytosponges (n=117) comprised: 46 normal esophagus, 44 non-dysplastic BE (NDBE), 10 low grade dysplasia, 10 high grade dysplasia and 7 inadequate samples.

ii) H&E slides of Cytosponges were used for an in-house computer vision tool assessment which uses deep learning to quantify distinct tissue phenotypes. Thus, the amount of columnar and squamous epithelium present in each section was calibrated. Differentially expressed miRNA markers were validated with qPCR and via computer vision tool in an independent cohort (n=139) with 68 inadequate and 71 adequate samples, of which 35 were normal and 36 NDBE.

Results: Four miRNAs candidates had statistically significant higher expression in diseased compared to healthy samples in the test cohort. We observed a positive correlation ($r=0.72-0.77$) between the expression levels of each miRNA and the amount of columnar epithelium from both the gastric and BE epithelium. All 4 markers were not expressed in inadequate samples which did not contain any type of columnar epithelium. An independent cohort of 139 cases validated these results, where all 4 miRNAs were differentially expressed in inadequate vs. adequate samples ($p=0.038-0.0001$). A 5-fold cross validation of the 4 miRNAs for sample adequacy in terms of the glandular cell content showed an AUC-ROC of 0.91. Hence, these markers were informative for the presence of any columnar epithelium (including BE) in the sample.

These results have considerable implications in the discovery of new markers in Cytosponge samples since orthogonal characterization of sampled material can avoid biases in selection of novel molecular biomarkers.

Conclusion: The expression of 4 miRNAs are a potential quality control tool for Cytosponge samples. A combined experimental and computer vision approach enabled the underlying biology of miRNA biomarker expression to be determined with relevance to other biomarker studies.

Disclosure: Rebecca C Fitzgerald is one of the named inventors on patents pertaining to the Cytosponge and related assays and is the co-funder of Cyted together with Marcel Gehrung. Neus Masque-Soler has no disclosures.

P0133

ETHNIC FEATURES OF THE BARRETT'S ESOPHAGUS WITH DYSPLASIA PREVALENCE IN THE POPULATION OF KHAKASSIA ADMINISTRATIVE CENTER

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Introduction: The incidence of esophageal cancer increasing rapidly in recent years, which makes actual the study of Barrett's esophagus (BE) [1].

Aims & Methods: From 2011 to 2015 in the endoscopic department of the republican hospital in Abakan were performed 11,615 endoscopic examinations in Caucasoids (5,537 men and 6,078 women, mean age 42.4 years), and 5,808 - in Khakas (2,774 men and 3,034 women, mean age 41.6 years) with video gastroscope Olympus GIF 180 using narrow-band imaging and magnifying technique. Heartburn was determined on the

basis of the Montreal consensus [2], BE - British Society of Gastroenterology guidelines [3]. Diagnosis of esophagitis was based on the Los Angeles Classification [4]. Barrett's esophagus and dysplasia were diagnosed using the morphological study. Daily pH monitoring was performed in 21 Khakases (10 men and 11 women) and 25 Caucasoids (12 men and 13 women) with heartburn.

Results: We found the predominance of prevalence of BE, weekly heartburn and esophagitis in Caucasoids compared with Khakases (Table). Heartburn in both populations was observed more frequently in patients with BE compared with persons without BE. The BE risk factors in Caucasoids and Khakases were male gender, increasing age and obesity. With daily pH monitoring, the average time with a pH < 4 during the day in the esophagus in Caucasoids with heartburn was 21.18±1.7%, in Khakases with heartburn - 15.5±1.3% (p=0.007). The number of alkaline refluxes also prevailed among alien inhabitants (25.1±1.7) compared with the indigenous population (19.4±1.4; p=0.01).

Conclusion: Ethnic differences of BE and esophagitis prevalence suggest that genetic factors may play a significant role in the pathogenesis of GERD.

Population	Weekly heartburn		Esophagitis		BE		BE with dysplasia	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
1. Caucasoids, n=11,615	1,440	12.4	486	4.2	163	1.4	28	0.24
2. Khakases, n=5,808	499	8.6	144	2.5	58	1.0	5	0.09
OR; 95% CI; p	1.5; 1.35-1.67; <0.001		1.71; 1.42-2.07; <0.001		1.40; 1.04-1.89; =0.03		2.60; 1.04-6.47; =0.04	

[The prevalence of BE, esophagitis and weekly heartburn in the population of Khakassia]

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Disclosure: Nothing to disclose

P0134

RADIOFREQUENCY ABLATION OF BARRETT'S ESOPHAGUS: THE REAL PRACTICE EXPERIENCE IN A TERTIARY HOSPITAL. IS IT THE BEST TECHNIQUE FOR THIS ENTITY?

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Introduction: Barrett's esophagus (BE) is a premalignant condition due to its capacity for progression to adenocarcinoma (EAC). Radiofrequency ablation (RFA) combined or not with other endoscopic procedures is the treatment of choice for BE. However, the risk of relapse exists in the medium term whether risk factors persist.

Aims & Methods: 1) To determine the efficiency of RFA of BE and the prevalence of adverse events in a tertiary Hospital.

2) To evaluate the risk factors associated with a year-relapse of BE post-RFA.

Prospective observational cohorts study about patients with BE treated with RFA in the endoscopy unit of University Clinical Hospital Lozano Blesa in Zaragoza from 2012 to 2019. Data were analyzed by SPSS Statistics 22.0.

Results: 50 patients with BE were included. Most of them were men (42/50; 84%) with a mean age of 56.44 ± 14.91 years old. Eight of them (8/50; 16%) without dysplasia, more than half with low-grade dysplasia (26/50; 52%), 18% with high-grade dysplasia (9/50), and 14% (7/50) with early cancer. The 92% (46/50) had a long length of Barrett segment (circumferential extent (C) 5.12 centimeters ± 3.63; maximum extent (M) 6.80 centimeters ± 3.00). Most of the patients had hiatal hernia (38/50; 76%). The patients underwent a median of 2 ± 1 RFA sessions, with a mean treatment time of 11.82 ± 10.76 months. Argon plasma coagulation (29/46; 58%) and multiband mucosectomy (12% (6/50)) were combined with RFA in most of the patients. There were any severity acute (during the procedure) or early (0-48 hours) complications such as perforation or death. However, there were 23% of mild complications including strictures (8/50; 16%) or mucosal ulcers (8/50; 16%). 41 of the 46 patients (92%) who ended the treatment were reevaluated after a year. Seven patients (14% (7/41)) had a recurrence of BE of which more than half needed Argon plasma coagulation (71.42% (5/7)), multiband mucosectomy was performed in 14.28% (1/7) and only one patient needed RFA (14.28%, 1/7). Most of BE recurrences were in males (5/7; 71.42%) with low-grade dysplasia (3/7; 42.85%). There were no significant association between the recurrence and the long length of Barrett segment (p=0.414) neither do high body mass index (more than 25) (p=0.117) nor sex (p=0.252). Some patients (8% (4/41)) had erosive esophagitis during the surveillance. Moreover, in three of them, Nissen's fundoplication was needed.

Conclusion: RFA in combination or not with other endoscopic procedures is highly effective near-term and has an excellent safety profile. However, long-term surveillance is highly recommended because the risk of recurrence is not negligible.

Disclosure: Nothing to disclose

P0135 WITHDRAWN

P0136

PROSPECTIVE MULTICENTRE RANDOMISED CONTROLLED TRIAL COMPARING THE SAFETY AND EFFECTIVENESS OF THE ENDOROTOR® MUCOSAL RESECTION DEVICE WITH CONTINUED ABLATION IN THE TREATMENT OF REFRACTORY BARRETT'S OESOPHAGUS: REPORT OF INITIAL OUTCOMES

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Introduction: Endoscopic ablation therapy is recommended in patients with flat dysplastic Barrett's oesophagus (BE). A proportion will be refractory to treatment. This is associated with neoplasia recurrence. The EndoRotor® device (Interscope Medical Inc, Whitinsville, MA, USA) is a non-thermal resection device. The aim was to compare the safety and efficacy of EndoRotor with ablation in the treatment of refractory BE.

Aims & Methods: This is an on-going prospective, randomised trial in two centres in the UK and USA. Patients with refractory BE were randomised to EndoRotor resection or continued ablation (Cryotherapy/Radiofrequency ablation). All patients had Intramucosal adenocarcinoma/High grade or Low-grade dysplasia at initial baseline histology. Patients were followed up every 3 months with a maximum of 3 treatments. Primary outcome was BE length reduction. Secondary outcomes included pain post procedure (pain scores), stricture rates and complications. Refractory disease was defined as the presence of BE after at least 3 sequential sessions of first line ablative endotherapy or less than 50% reduction in BE after two sessions.

Results: A total of 11 patients were recruited thusfar. 5 randomised to EndoRotor and 6 to ablation.

In the EndoRotor arm the mean initial BE length was C 1.4 (SD 2.1) and M 3.5 (SD 1.9). Patients had a median number of 5 (IQR, 3-6) previous ablations. Patients had a mean of 2 EndoRotor procedures. The mean BE length post initial treatments is C 1 and M 1.9 thusfar. There were 14 procedures performed. Patients had mild (score =1- 4) discomfort post 3/14 procedures. There were no perforations/strictures during follow-up. There was one adverse event where intraprocedural bleeding was treated successfully with bipolar probes.

In the ablation arm the mean baseline initial BE length was C 0.7 (SD =1.2) and M 3.6 (SD 1.9). They had a median number of 4 (IQR, 3-5) previous ablations. They had a mean of 2 follow-up ablations. The mean current BE length post treatment is C 0.2 and M 3.2. There were 13 procedures performed. There was one report of mild discomfort post procedure.

	EndoRotor arm (N = 5)	Ablation arm (N = 6)
Median no. of previous ablations	5 (IQR, 3-6)	4 (IQR, 3-5)
Median number of procedures	2	2
Median follow up time (months)	6 (IQR, 3-6)	5 (IQR, 3-6)
Median procedure treatment time (Mins)	32 (IQR, 16-60)	6 (IQR, 5-9)
Median reduction in BE length (C) (mm)	4	5
Mean reduction in BE length (M) (mm)	16	4

[Table 1: Outcomes in the EndoRotor and ablation arm]

Conclusion: EndoRotor is safe to use in the treatment of refractory BE with no associated strictures and low pain scores. In this cohort of refractory patient's EndoRotor has slightly better outcomes in terms of BE length reduction. This data will be validated with more patients recruited and completed treatment sessions with histology and final BE lengths.

Disclosure: Laurence B Lovat: Minor shareholder in Odin Vision. Research grants from Medtronic, Pentax Medical, DynamX. Scientific Advisory Boards: Dynamx, Odin Vision, Ninepoint Medical. Rehan Haidry: Received Educational grants to support research from Medtronic Ltd., Cook Endoscopy (fellowship support), Pentax Europe, C2 Therapeutics, Beamline diagnostics.

P0137

PROSPECTIVE EVALUATION AND SCREENING GUIDELINES FOR BARRETT'S ESOPHAGUS

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Introduction: Recent guidelines recommending Barrett's Esophagus (BE) screening in selected patients with multiple risk factors have never been prospectively tested. We have initiated a multi-center study to detect BE in subjects who meet new screening guidelines and evaluate a novel non-endoscopic method for BE detection.

Aims & Methods: Patients with > 5 years of GERD over age 50 referred to gastroenterologists at 6 institutions are eligible either if they are white men or if they have three additional risk factors for esophageal adenocarcinoma (male gender, obesity, white race, smoking, family history). Those undergoing EGD are asked to undergo a non-endoscopic diagnostic test using Esocheck (Lucid Diagnostics, PavMed Inc.), a swallowable encapsulated balloon device that samples the distal esophagus. BE and esophageal adenocarcinoma (EAC) are detected by assaying DNA extracted from the distal esophagus for methylated VIM and CCNA1.

Results: BE has been detected in 6 (8.7%) of the 69 subjects who were eligible for study. Mean age of subjects is 60.4 years, 47 (68%) are men, and 60 (87%) are white. Thirty seven subjects agreed and had the non-endoscopic encapsulated balloon test performed. The Esocheck sampling test took less than five minutes, was well tolerated, and could be performed by non-physicians as well as physicians. Preliminary methylated DNA marker assay results available on 20 subjects detected all 3 subjects with BE (100% sensitivity), was positive in 1 individual with intestinal metaplasia of the cardia, and was negative in 15 of 16 normal subjects (94% specificity).

Age (mean (SD))	60.31(10.35)
Male Gender (n (%))	47 (68.1%)
Female Gender (n (%))	22 (31.9%)
White Race	60 (87%)
African Americans Race	9 (13%)
Smoking History	45 (69%)
BMI	31.25 (6.77%)
Antacid Use	61 (88%)
Family history of BE	4 (6%)
Agreed to had the non-endoscopic encapsulated balloon test	37 (53.6%)

[Table1: Demographics Characteristics]

Conclusion: To date EGD has detected BE in nearly 1 of 11 eligible subjects identified prospectively, confirming the validity of using screening guidelines. The Esocheck encapsulated balloon based distal esophageal sampling device coupled with methylated DNA markers demonstrates the feasibility of unsedated non-endoscopic office-based BE screening. This study is ongoing.

Disclosure: Nothing to disclose

P0138

FIRST IN-HUMAN STUDY ON THE SAFETY, TOLERABILITY AND EFFICACY OF THE AQUAMEDICAL FOCAL RF-VAPOR ABLATION (RFVA) SYSTEM, FOR THE ERADICATION OF BARRETT'S ESOPHAGUS (BE): THE STEAM-BE DOSIMETRY STUDY

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Introduction: Radiofrequency ablation (RFA) is the preferred modality for ablation of dysplastic BE. Although highly effective, RFA has drawbacks such as multiple deployment steps; the need for direct contact with the esophageal wall; and generally multiple treatment sessions are required. Aqua RFVA System (AquaMedical, Inc.) is a novel ablation system that generates water vapor at 100°C using an RF electrode to ablate tissue. It is a through-the-endoscope technique that acts without direct contact with the esophageal wall. We studied dosimetry using in-vitro lean-beef and porcine models and tested the feasibility, safety and efficacy in patients with flat dysplastic BE.

Aims & Methods: Aqua system includes an RFVA generator (60W), a 7Fr RFVA catheter and a syringe with saline. The catheter is passed through the biopsy channel of a standard endoscope and works in conjunction with a distal attachment cap to create focal (~1 cm²) ablations in the esophagus. The Aqua system was tested in 3 successive phases; a lean-beef model; a porcine study (n= 6); and a first in-human study (n=15). In the lean-beef and porcine study, ablation depth at different dosages Vapor (dose = duration in seconds) was compared with focal RFA (1-4x 12J/cm²) at acute (0h) and subacute (48h) setting. Two doses were selected for further human testing in patients with flat dysplastic BE with 4 ablations (2 per dose) per patient. Patients were followed post-ablation for symptoms and adverse events. Follow-up endoscopy with histology was performed after 8 weeks to assess the proportion of squamous conversion for each treatment area.

Results: None of the treatments in all study-phases resulted in any complications. As expected, in the lean-beef model (total 40 ablations), increasing doses of Vapor and RFA both resulted in deeper ablation. 2-5sec Vapor resulted in a mean depth ranging from 0.8 to 1.5mm, and was comparable to 1-4x 12J/cm² RFA (range 0.6-1.5mm). In the acute porcine evaluation, no differences were found for all doses and treatments tested. Vapor at 3 and 5 seconds (total 42 ablations) and 1-2x 12J/cm² RFA resulted in mean ablation depth of 0.48, 0.53, 0.49 or 0.50mm, respectively. However, as the treatment effect evolved over 48h (total 60 ablations), Vapor at 3 seconds dose (0.56mm) was comparable to 2x 12J/cm² RFA (0.45mm), whereas Vapor at 5 seconds produced slightly deeper ablation (0.72mm). We selected a conservative 1 & 3 seconds dose for the human study. A total of 60 ablations were technically successful applied in 15 patients. No adverse events occurred and the procedure was well-tolerated, with pain scores ranging from 0-2 out of 10 during 14 days post treatment. Follow-up endoscopy

showed a median squamous conversion rate of 55% (IQR 13-91) for 1 second and 98% (IQR 61-100) for 3 seconds. All biopsies from endoscopically eradicated areas contained normal squamous epithelium without buried BE glands.

Conclusion: In this 3-phase study with lean-beef, porcine and the first in-human application, the Aqua RFVA system was safe for focal esophageal ablation and successfully converted dysplastic BE into squamous epithelium. These preliminary yet promising results warrant further testing with RFVA devices.

Disclosure: This study was financially supported by Aqua Medical, Inc.

P0139 WITHDRAWN

P0140

POOR HEALING AND POOR SQUAMOUS REGENERATION AFTER RADIOFREQUENCY ABLATION THERAPY FOR EARLY BARRETT'S NEOPLASIA: INCIDENCE, RISK FACTORS, AND OUTCOMES

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Introduction: Although endoscopic eradication therapy (EET) with radiofrequency ablation (RFA) is effective in the majority of patients with Barrett's Esophagus (BE), a subgroup of patients is unable to achieve complete eradication of BE. Some might experience delayed healing with visible ulcerations after RFA ("poor healing"; PH) and/or regeneration with BE mucosa ("poor squamous regeneration"; PSR). Little data is available for PH/PSR and practical recommendations are lacking. We aimed to evaluate the incidence, risk factors, and outcomes of patients with PH/PSR after RFA.

Aims & Methods: We included all patients with at least 1 RFA treatment from a nationwide registry in the Netherlands with all patients who underwent EET for early BE neoplasia. All treatments were performed by specifically trained endoscopists according to a joint treatment and follow-up protocol. PH was defined as visible ulcerations ≥3 months post-RFA; PSR as < 50% regression 3 months after RFA. Treatment success was defined as a complete eradication of BE (CE-BE).

Results: 1,386 patients were included with a median BE length of C2M5 containing LGD (27%), HGD (30%), or early cancer (43%) as worst histology. PH occurred in 10% of patients (134/1,386) and additional time +/- acid suppression resulted in complete healing in all patients. Upon complete healing, normal squamous regeneration was seen in 50% (67/134), 97% of which (65/67) achieved CE-BE. Overall, 5% of patients had PSR (74/1,386),

which was preceded by PH in 92% (67/74). 64% (47/74) of PSR patients failed CE-BE. 70% (33/47) of failures were free of neoplasia with 30/33 undergoing endoscopic follow-up. During mean 42 months 23% (7/30) progressed to early neoplasia all of which underwent curative endoscopic treatment. The remaining 30% of failures (14/47) had persisting neoplasia (HGD+). Overall, patients with PSR had a higher risk for progression to advanced cancer that exceeded boundaries for endoscopic treatment as compared to patients without PSR (15% vs. < 1% resp., $P < 0.01$). Risk factors for PSR include < 50% squamous regeneration after baseline endoscopic resection (odds ratio (OR) 13.1 [95% confidence interval 6.8-25.9]), presence of reflux esophagitis (OR 7.1 [2.9-16.6]), longer BE segments (OR 1.3 [1.2-1.4]), and higher BMI (OR 1.1 [1.0-1.2]).

		No PH or PSR N=1,245	PH, no PSR N=67	PSR ± PH N=74	P-value
Treatment characteristics	Treatment duration, months, median (IQR)	8 (4-13)	15 (10-20)*	14 (7-23)*	<0.01
	Circumferential RFA, n, mean (±SD)	0.6 (0.6)	0.8 (0.8)	1.4 (0.7)*	<0.01
	Focal RFA, n, mean (±SD)	1.6 (1)	1.9 (1)	1.4 (1)	0.3
	Endoscopic resection endoscopies, n, mean (±SD)	0.7 (0.7)	0.8 (0.9)	1.1 (1)*	<0.01
	Pop-up lesion, n (%)	61 (5)	7 (10)	16 (22)*	<0.01
	Esophageal stenosis, n (%)	168 (14)	23 (34)*	19 (26)*	<0.01
Treatment outcomes**	CE-BE, n (%)	1178 (98)	65 (97)	27 (37)*	<0.01
	Treatment failure, n (%)	29 (2)	2 (3)	47 (63)*	<0.01
	Progression to advanced cancer, n (%)	6 (<1)	0 (0)	11 (15)*	<0.01

*Is statistically different from no PH/PSR group after Bonferroni correction.
 **Overall, in 38 patients treatment was prematurely ended due to unrelated, severe new comorbidity (n=21), or unrelated death (n=17).

[Table 1. Treatment characteristics and outcomes.]

Conclusion: PH and/or PSR occurs in 10% of patients after RFA. PH may be managed with additional time and acid suppression. Half of the patients will then have normal squamous regeneration with excellent success rates. On the other side, patients with PSR have a high risk for treatment failure and progression to advanced disease during RFA. Therefore, upon detection of PSR, continuation of ablative therapy should be reconsidered and carefully balanced against alternative treatment options. Endoscopic surveillance is a valid alternative in remaining BE with no neoplasia, whereas esophagectomy may be considered at early stages if advanced neoplasia is present.
Disclosure: Nothing to disclose

P0141 GLOBAL PREVALENCE OF BARRETT’S OESOPHAGUS AND OESOPHAGEAL CANCER IN INDIVIDUALS WITH GASTRO-OESOPHAGEAL REFLUX: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Chronic gastro-oesophageal reflux might lead to the development of Barrett’s oesophagus (BO), or even oesophageal adenocarcinoma. There has been no definitive systematic review and meta-analysis of data to estimate global prevalence of BO or oesophageal adenocarcinoma in individuals with gastro-oesophageal reflux.
Aims & Methods: We searched MEDLINE, EMBASE, and EMBASE Classic to identify cross-sectional surveys that reported prevalence of BO or oesophageal adenocarcinoma in adults with gastro-oesophageal reflux. We extracted prevalence for all studies, both for endoscopically suspected, and histologically confirmed, cases. We calculated pooled prevalence, according to study location, symptom frequency and sex, as well as odds ratios (ORs), with 95% confidence intervals (CIs).

Results: Of the 4,963 citations evaluated, 44 reported prevalence of endoscopically suspected and/or histologically confirmed BO. Prevalence of BO among individuals with gastro-oesophageal reflux varied according to different geographic regions ranging from 3%-14% for histologically confirmed BO, with a pooled prevalence of 7.2% (95% CI 5.4%-9.3%), whereas pooled prevalence for endoscopically suspected BO was 12.0% (95% CI 5.6%-20.4%). Prevalence of BO was significantly higher in men, both for endoscopically suspected (OR = 2.1; 95% CI 1.6-2.8) and histologically confirmed BO (OR = 2.3; 95% CI 1.7-3.2). Dysplasia was present in 13.9% (95% CI = 8.9%-19.8%) of cases of histologically confirmed BO, 80.7% of which was low-grade. Oesophageal adenocarcinoma was present in 1.2% (95% CI 0.3%-2.9%) of BO cases.

Conclusion: The prevalence of Barrett’s oesophagus among individuals with gastro-oesophageal reflux varied strikingly among countries, broadly resembling the geographic distribution of gastro-oesophageal reflux itself. Prevalence of BO was significantly higher in men.
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Disclosure: Nothing to disclose

P0142 WITHDRAWN

P0143

BARRETT'S ESOPHAGUS WITH DYSPLASIA: IMPACT OF THE REFERRAL TO A SPECIALIZED CENTER

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Introduction: Barrett's esophagus (BE) is a premalignant condition predisposing to esophageal adenocarcinoma (EAC). Esophageal mucosal lesions in this context are often subtle and challenging to identify. Therefore, any degree of dysplasia in BE should be referred to a BE expert center for confirmation by an expert gastrointestinal (GI) pathologist since the majority of patients will be downstaged.

Aims & Methods: To evaluate the overall change in the diagnosis and degree of dysplasia and the number of patients with visible lesions (VL) in BE patients with flat dysplasia, referred to our institution. We also aimed to evaluate the management and clinical course of these patients.

A cohort study was conducted in BE patients with flat dysplasia referred to our centre between January 2016 - February 2020. Histopathological review and endoscopic revaluation were performed. If no VL were found, biopsies were taken according to Seattle protocol.

Results: A total of 24 patients were referred (male: 83.3%; age - 66.5±10.6 years). At the referral, median circumferential (C) extent using Prague criteria was 2.9 cm (range: 0-9cm) and median maximum (M) extent was 4.4cm (range: 1-10cm). Dysplasia grade was as follows: indefinite for dysplasia (IND) - 3; Low grade dysplasia (LGD) - 17 (multifocal-2); multifocal LGD + high grade dysplasia (HGD) - 2; multifocal LGD+HGD+EAC - 1. Following histological review, 54.2% (n=13) of cases were downstaged to non-dysplastic BE (NDBE) or IND. In 12.5% (n=3) there was upstage to HGD. In the remaining cases, initial dysplasia grade was confirmed (IND - 3, LGD - 3, HGD - 1, EAC - 1).

After endoscopic revaluations at our institution VL were found in 11 patients (45.8%) (median size: 12.7±7.4mm, Paris classification: 0-Is-4; 0IIa-4; 0-IIb-2; 0-Is+0-IIa-1; 0-IIb+0-IIc-1; not specified-4; histology of the biopsies performed: NDBE - 1, IND - 2, LGD - 7, HGD - 3, LGD+HGD - 1, EAC - 2). From those patients in whom no VL were found, only 2 presented IND and the remaining downstaged to NDBE. In these 2 patients, antireflux medication was optimized and endoscopy repeated 6 months later. VL were once again not found and biopsy samples showed again IND. Patients classified as NDBE after revaluation were put under a surveillance program according to the length of the BE.

The group of patients with VL, 10 were treated by Band Ligation Endoscopic Mucosal Resection (L-EMR) and 1 is waiting for endoscopic treatment. L-EMR was technically successful in 90.0% (9/10) of the cases (histology of the specimens: NDBE - 1, LGD - 2, HGD - 2, EAC - 5 [pT1a - 4, pT1b - 1]). One patient underwent esophagectomy after non-curative L-EMR (EAC).

Eradication of all remaining Barrett's epithelium using radiofrequency was accomplished in 6 patients, and 1 patient is completing the eradication program. In the other 2 patients, only residual islands remained after L-EMR.

During endoscopic follow up (median time: 16.6±14.0 months), recurrence of VL (HGD) occurred in one patient, being endoscopically managed.

Conclusion: Histological revision by expert GI pathologist resulted in the downstage to NDBE or IND in more than half of the patients. Moreover, systematic evaluation of BE segment by BE experienced endoscopist increased the detection of early esophageal lesions, further allowing curative endoscopic treatment in the majority of the cases. Our results are in agreement with ESGE recommendations regarding the referral of BE with dysplasia to specialized centers.

Disclosure: Nothing to disclose

P0144

GENETIC VARIATION FROM ESOPHAGEAL SQUAMOUS CELL CARCINOGENESIS TO POST-TREATMENT REGENERATED MUCOSA

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Introduction: Recently genetic mutations in esophageal squamous cell carcinoma (SCC) and also in the background mucosa have been gradually clarified reported. However, genetic characteristics post-treatment regenerated mucosa after endoscopic resection is still not fully understood. In this study, we aimed to elucidate genetic variation in the process from esophageal squamous cell carcinogenesis to post-endoscopic treatment scar.

Aims & Methods: Group A :

As a healthy control, esophageal mucosal tissues were collected from five controls without Lugol voiding lesions in esophagus.

Group B :

Tissues from both SCC and background mucosa were collected from 14 patients who underwent endoscopic submucosal dissection (ESD) for esophageal SCC. In 7 of these cases, tissue was collected from the post-ESD scar at the time of upper endoscopic surveillance.

We extracted DNA from these tissues and performed next-generation sequencing using a system that targets all exon regions of 70 esophageal cancer-related genes to identify somatic mutations. We also checked whether each mutation was oncogenic or not concerning OncoKB.

Results: Group A :

Out of 5 healthy controls, 2 patients have no somatic mutation, and 3 controls have some somatic mutations without oncogenic mutations. NOTCH1 mutation as detected in that 3 controls and the most frequent somatic mutation between healthy controls.

Group B :

TP53 mutation was the most frequent mutation in SCC (13/14, 93%), on the other hand, NOTCH1 mutation was the most frequent mutation in background mucosa (93% in 13 cases). We confirmed At least one somatic mutation in all specimens of SCC and background mucosa. In only 7 cases in which post-endoscopic resection scar tissue could be obtained, 21 mutations in 11 genes were identified in SCC, 34 mutations in 20 genes in scar, and 66 mutations in 23 genes in background mucosa. The allele frequency (%) of mutations was significantly higher in SCC (33[3-81] vs 23[3-63] vs 8[3-78], p=0.002). 7 mutations in 5 cases in SCC, 1 mutation in 1 case in scar, and 4 mutations in 3 cases in background mucosa were oncogenic. In scar, 4 cases had NOTCH1 mutations, the most frequent mutation, and 3 cases had overlapped somatic mutations in the scar and background mucosa. In contrast, no mutation was found in scar in only 1 case.

Conclusion: Unlike the population with a high risk of esophageal SCC, there were some cases with no somatic mutation in the background mucosa of healthy controls. Judging from these results, it was assumed that exposure to risk factors like smoking or alcohol intake would increase the somatic mutation in the background mucosa. Moreover, these accumulated mutations could cause carcinogenesis.

On the other hand, at the healing phase after endoscopic resection, somatic mutations were partially or fully cancelled in some cases during the process leading to scar. However, almost all of regenerated mucosa had

any somatic mutations, which were thought to be caused by the regeneration of cells carrying mutations accumulated in the background mucosa. In the case of esophageal SCC, the regenerated mucosa may also reflect the genetic mutations in the background mucosa.

Disclosure: Nothing to disclose

P0145

IS LOCAL ENDOSCOPIC RESECTION A VIABLE THERAPEUTIC OPTION FOR EARLY CLINICAL STAGE T1A AND T1B OESOPHAGEAL ADENOCARCINOMA? A PROPENSITY-MATCHED ANALYSIS

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Introduction: The role of endoscopic resection (ER) in the management of subsets of clinical T1N0 oesophageal adenocarcinoma is controversial. The aim of this study was to evaluate the outcome of ER versus oesophagectomy in node negative cT1a and cT1b oesophageal adenocarcinoma.

Aims & Methods: Data from the National Cancer Database (2010-2015), was used to identify patients with clinical T1aN0 (n=2,545) and T1bN0 (n=1,281) oesophageal adenocarcinoma that received either ER (cT1a, n=1,581; cT1b, n=335) or oesophagectomy (cT1a, n=964; cT1b, n=946). Propensity score matching (PSM) and Cox multivariable analyses were used to account for treatment selection bias.

Results: ER for cT1a and cT1b disease was performed more commonly over time. The rates of node-positive disease in patients with cT1a and cT1b oesophageal adenocarcinoma were 4% and 15%, respectively. In the matched cohort for cT1a cancers, ER had similar survival to oesophagectomy (HR: 0.85, 95% CI: 0.70-1.04, p=0.1). The corresponding 5-year survival for ER and oesophagectomy were 70% and 74% (p=0.1), respectively. For cT1b cancers, there was no statistically significant difference in overall survival between the treatment groups (HR: 0.87, 95% CI: 0.66-1.14, p=0.3). The corresponding 5-year survival for ER and oesophagectomy were 53% vs. 61% (p=0.3), respectively.

Conclusion: This study demonstrates ER has comparable long-term outcomes for clinical T1aN0 and T1bN0 oesophageal adenocarcinoma. However, 15% of patients with cT1b oesophageal cancer were found to have positive nodal disease. Future research should seek to identify the subset of T1b cancers at high risk of nodal metastasis and thus would benefit from oesophagectomy with lymphadenectomy.

Disclosure: Nothing to disclose

P0146 WITHDRAWN

P0147

EVALUATION OF THE RELATIONSHIP BETWEEN SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA AND HUMAN PAPILLOMA VIRUS TOGETHER WITH GENETIC POLYMORPHISMS OF ADH1B AND ALDH2

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Introduction: It is well known that an alcohol consumption habit together with inactive heterozygous ALDH2 is an important risk factor for the development of esophageal squamous cell carcinoma (ESCC). However, some patients with ESCC do not drink or only occasionally drink alcohol. The hypothesis that human papilloma virus (HPV) infection can cause ESCC was proposed more than two decades ago; however, it remains controversial whether HPV infection contributes to the occurrence/development of ESCC. There has been no study in which the relationship between ESCC and HPV in addition to ADH1B/ALDH2 genotype was evaluated.

Aims & Methods: The aim of this study was to clarify the carcinogenic risk of HPV infection for superficial ESCC. In this study, we also evaluated ADH1B/ALDH2 genotype and smoking and alcohol consumption histories. We conducted an exploratory retrospective study using new specimens, and we enrolled 145 patients who underwent endoscopic resection for superficial ESCC and had been observed for more than two years by both physical examination and endoscopic examination in Hokkaido University Hospital. We obtained information on smoking and alcohol consumption histories by using a questionnaire. We also obtained information on the occurrence of metachronous multiple esophageal/head and neck cancer after initial treatment. Buccal mucosa was collected from all patients by using a cotton swab before endoscopic examination to analyze genetic polymorphisms of ADH1B/ALDH2. We performed in situ hybridization for resected specimens to detect HPV by using an HPV type 16/18 probe.

Results: HPV was detected in 15 (10.3%) of the 145 patients with ESCC. HPV-positive rates in inactive ALDH2 *1/*2 and ALDH2 *1/*1 + *2/*2 were 10.8% and 9.8%, respectively (p = 0.83). HPV-positive rates in slow-metabolizing ADH1B *1/*1 and ADH1B *1/*2 + *2/*2 were 12.0% and 10.0%, respectively (p = 0.77). HPV-positive rates in the heavy or moderate alcohol consumption group and the light or rare consumption group were 11.1% and 8.7%, respectively (p = 0.65). HPV-positive rates in the heavy smoking group and the light or no smoking group were 11.8% and 8.3%, respectively (p = 0.50). There were no significant differences in HPV-positive rates according to either ADH1B/ALDH2 genotype or smoking and alcohol consumption histories. The 5-year incidence rates of secondary esophageal/head and neck cancer after initial treatment in the HPV-positive and HPV-negative groups were 14.4% and 35.0%, respectively (p = 0.22).

Conclusion: In conclusion, our study in which genetic polymorphisms of ADH1B/ALDH2 were considered suggested that HPV did not have an association with ESCC. In the present situation, HPV status is considered to be less important than other risk factors, such as alcohol consumption, smoking habit, and ADH1B/ALDH2 polymorphisms, and HPV status would therefore have no effect on ESCC risk management.

Disclosure: Nothing to disclose

P0148 WITHDRAWN

P0149

ENDOSCOPIC REASSESSMENT OF CT2N0M0 ESOPHAGEAL ADENOCARCINOMA LEADS TO DOWNSTAGING TO T1 TUMORS AND PREVENTS UNNECESSARY ADJUVANT TREATMENT: A MULTICENTER PROSPECTIVE COHORT STUDY

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Introduction: The clinical tumor stage in esophageal adenocarcinoma (EAC) is usually based on endoscopic ultrasound (EUS) or CT-scan. Unfortunately, the accuracy of EUS and CT differentiating between T1 and T2 EAC is low (43-55%). A substantial number of patients with pT1 stage are overstaged as cT2. As a result, these patients unnecessarily undergo more invasive treatment, such as chemoradiotherapy and surgery.

Aims & Methods: Our aim was to assess the proportion of cT2 EACs downstaged to cT1 after endoscopic reassessment. We performed a prospective multicenter cohort study in five esophageal cancer expert centers in the Netherlands. All consecutive patients with cT2N0M0 EAC diagnosed between April 2018 and April 2020 were asked to participate. Exclusion criteria were presence of esophageal stenosis limiting endoscopic resection. Patients underwent endoscopic reassessment by an experienced interventional endoscopist who was expert in performing endoscopic resection in the esophagus. If endoscopic reassessment suggested a cT1 tumor, the patient was treated with an endoscopic resection. The primary endpoint was the proportion of cT2 EAC patients in which the tumor was downstaged to cT1 after endoscopic reassessment.

Secondary endpoints were the proportion of patients who were successfully treated with endoscopic resection after endoscopic reassessment, and the proportion of curative endoscopic resected pT1 EACs based on the accepted criteria (pT1 EAC with invasion depth limited to 500 µm of the submucosa in combination with good or moderate tumor differentiation, and no lymphovascular invasion).

Results: A total of 25 patients were included. The median diameter of the tumor was 30mm (IQR 20-45). Endoscopic reassessment resulted in downstaging from T2 to T1 EAC in 16/25 (64%) patients whom all underwent an attempt at endoscopic resection. Endoscopic resection was not successful in 4/16 patients due to tumor invasion in the muscle layer. Twelve of sixteen (75%) patients underwent a successful endoscopic resection and all were proven by pathological examination to be pT1 tumors.

Of these 12 patients, 5/12 (42%) resected pT1 tumors were within the accepted criteria for curative endoscopic resection, 2/12 (17%) patients received adjuvant treatment (definitive chemoradiotherapy in one patient and esophagectomy in another patient), and in 5/12 patients a wait-and-see strategy was chosen based on patients preference.

In the remaining 9/25 (36%) patients, endoscopic reassessment confirmed a T2 tumor stage based on the presence of invasive features (e.g. depressed lesion, ulceration). Overall, with a strategy of endoscopic (re-) assessment of suspected tumor stage, 12/25 (48%) cT2 EACs turned out

to be histologically proven pT1 EACs. Therapeutic management changed for all 12 patients and 10/25 (40%) patients were treated with endoscopic resection only.

Conclusion: In patients with a cT2 EAC according to CT/EUS assessment, endoscopic reassessment by an experienced interventional endoscopist downstages about half of the cases to a T1 tumor suitable for endoscopic resection. This has a substantial clinical impact on therapeutic management with endoscopic reassessment preventing adjuvant treatment in 40% of patients. Based on these results, we recommend endoscopic reassessment by an experienced interventional endoscopist for all cT2N0M0 staged EAC patients.

Disclosure: Nothing to disclose

P0150

SCREENING ENDOSCOPY IS USEFUL FOR DIAGNOSIS OF EARLY ESOPHAGEAL CANCER IN ASYMPTOMATIC MALES

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Introduction: Prognosis of esophageal cancer (EC) is poor, because most EC are diagnosed at advanced stage in clinical practice. Recently, gastric cancer mortality has been decreasing in Japan, but EC mortality has been increasing. Therefore, early detection for EC is required in asymptomatic subjects. EC is characterized by adult males, and history of drinking and smoking are riskfactors. In addition, recent studies indicate that atrophic gastritis is also a risk factor for esophageal squamous cell carcinoma (ESCC).

Aims & Methods: We investigated the prevalence of EC in asymptomatic 53,640 subjects over 50 years old who had the screening esophagogastroduodenoscopy (EGD) at our Health Care Center during Apr 2016 to Mar 2019. In addition, a case-control study was performed on mean corpuscular volume (MCV), body mass index (BMI), smoking status, alcohol consumption, and the presence of atrophic gastritis. The association between EC and controls was assessed by chi-square test.

Results: Among a total of 53,640 subjects, 25 EC patients (24ESCC and one adenocarcinoma, median age; 66.2 ± 7.3) were detected and the prevalence was 0.05%. All EC patients were diagnosed in the early stage. 24 of 25 EC patients were male and the prevalence of EC in male subjects was 0.09% (24/27454). Investigating the prevalence by age in male subjects, it was 0.06% in the 50s, 0.07% in 60s, 0.15%, in 70s, and 0.1% in 80s. In the annual trend, it was 0.03% in 2016, 0.02% in 2017, and 0.06% in 2018 and the percentage increased in 2018. From the results of a case-control study of 75 healthy male subjects of age-matched EC, significant differences were observed on MCV > 100 ($p=0.0003$), in smoking status ($p=0.01$) and in alcohol consumption ($p=0.001$), whereas no difference was found in BMI and the presence of atrophic gastritis between the two groups.

Conclusion: Screening endoscopy for EC is useful in asymptomatic males over 50 years, and MCV in peripheral blood and the history of smoking and drinking is effective to select the subjects. Atrophic gastritis was not associated with ESCC. Prevalence of esophageal adenocarcinoma was still low in Japan.

Disclosure: Nothing to disclose

P0151

ACCURACY OF ESOPHAGEAL CANCER GRADE ON PREOPERATIVE BIOPSIES COMPARED TO POST RESECTION PATHOLOGY

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Introduction: Endoscopic resection (ER) of early esophageal adenocarcinoma (EAC) is recommended for tumors with a low risk of lymph node metastasis (LNM). High risk histopathologic features of LNM, including poor differentiation, lymphovascular invasion, and deep submucosal invasion, are better treated with esophagectomy. Poorly differentiated pathology on pre-operative esophagogastroduodenoscopy (EGD) biopsies may deter endoscopists from performing ER. Determination of tumor grade can be affected by tissue sample size, which is smaller when obtained from EGD biopsies compared to ER or esophagectomy.

Aims & Methods: We aim to identify the accuracy of EAC grade on EGD mucosal biopsy compared to endoscopically or surgically resected tissue. A multicenter, retrospective analysis included patients with EAC on pre-operative EGD biopsies that underwent ER or esophagectomy from 2010-2019. Pathology reports, reviewed by expert gastrointestinal pathologists, were used to compare pathologic differentiation between preoperative EGD biopsies and either EMR, ESD, or esophagectomy specimens.

Results: We identified 262 patients with postresection pathology showing EAC (108 ER, 154 esophagectomy) with preoperative biopsies in our system from 2010-2019. The overall accuracy of tumor grade on preoperative biopsies compared to tissue from ER or esophagectomy was 73.8% (93/126) after excluding marked architectural distortion (MAD), unknown differentiation, or high-grade dysplasia (HGD) on preoperative biopsy. Assuming unknown differentiation or MAD on preoperative biopsies were moderate differentiation⁴, overall accuracy of preoperative biopsies for tumor grade was 66.5% (145/218).

Of 87 patients with preoperative biopsies showing poor differentiation, postresection pathology was congruent in 78.1% (68/87) and down-staged to moderate differentiation in 21.8% (19/87) of patients. Moderately differentiated tumors were up-staged to poor differentiation in 7 of 34 (20.6%) patients. Of 44 pre-operative biopsies showing HGD Barrett's and EAC on postresection pathology, 8 (18.2%) were up-staged to poorly differentiated tumors. In those with unknown differentiation on preoperative EGD, 18.1% (3/16) of patients were found to have poorly differentiated cancer. ESD and EMR had an overall congruence of 77.8% and 37.5%, respectively, when excluding biopsies with MAD, unknown differentiation, or HGD. ESD down-staged 1 of 8 (12.5%) patients from poor to moderate differentiation, and up-staged 1 of 9 (11.1%) patients from HGD to poorly differentiation. EMR upstaged 3 of 30 (10%) patients with HGD on preoperative biopsy to poorly differentiated EAC after resection. EMR down-staged 1 of 2 (50%) poorly differentiated tumors to moderate differentiation.

The overall congruence of preoperative EGD biopsies and postresection tissue was 42.9% and 68.8% in T1a and T1b tumors, respectively. In T1a tumors, esophagectomy and EMR down-staged 44.4% (4/9) of poorly differentiated tumors to moderate differentiation. Overall accuracy increases to 11/16 (68.8%) in T1b tumors, and esophagectomy and ESD down-staged 2 of 11 (18.2%) patients from poor to moderate differentiation.

Conclusion: In this study, the overall accuracy of preoperative EGD biopsies compared to ER or esophagectomy is only ~55%. Poorly differentiated tumors were down-staged to moderate differentiation in 21.8% on overall post-resection pathology, 44.4% of T1a tumors, and 18.2% of T1b tumors. Poorly differentiated EAC pathology on pre-operative biopsies should not preclude endoscopic resection, especially in poor surgical candidates, where staging ESD could be considered.

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Disclosure: Nothing to disclose

P0152

SCREENING FOR SYNCHRONOUS SECOND PRIMARY ESOPHAGEAL TUMOR IN PATIENTS WITH HEAD AND NECK CANCER

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Introduction: Patients with head and neck squamous cell carcinoma (HNSCC) have an increased risk of developing a second primary tumor (SPT) in the esophagus. A systematic review of multiple screening studies in mostly Asian populations with HNSCC showed a pooled prevalence of esophageal SPT of 15%. However, the incidence of esophageal SPTs in HNSCC patients in the Western population is still unclear.

Aims & Methods: Our aim was to determine the incidence of synchronous esophageal SPTs in patients with HNSCC in a Western country. We performed a prospective screening study in a tertiary hospital in the Netherlands. All patients diagnosed with HNSCC between February 2019 and February 2020 were eligible.

Inclusion criteria were HNSCC in the oropharynx (HPV negative), hypopharynx, or in any other head and neck sub-location in combination with alcohol abuse (male >15 units/week, female >7 units/week). Exclusion criteria were history of esophageal squamous cell carcinoma (ESCC) or contraindications for esophagogastroduodenoscopy (EGD).

Included patients underwent endoscopic screening using white light, narrow-band imaging and Lugol chromoendoscopy by an experienced interventional endoscopist during work-up for HNSCC, within two weeks after HNSCC diagnosis. SPT was defined as ESCC or high grade dysplasia, according to the Vienna classification of gastrointestinal epithelial neoplasia.

Results: Out of 123 eligible patients, 30 patients were excluded because of the following reasons: the patient declined to participate (n=22), HNSCC treatment was palliative (n=4), the patient was in poor condition (n=3), or general anesthesia was required for EGD (n=1). Ninety-three patients were included, 81% (n=75) was male, median age was 66 years (IQR 59-70), and 77% used alcohol (median of 21 units/week; IQR 16-40). The majority of HNSCC were located in the oropharynx (33%), hypopharynx (30%) or larynx (20%). In 67/93 (72%) patients no SPT was detected. In 26/93 patients (28%) a lesion was found with a low threshold suspicion for SPT. In 14/26 patients (54%) subsequent biopsy (n=11) or endoscopic mucosal resection (EMR) (n=3) did not confirm an SPT. In 2/26 patients, Lugol voiding lesions suspected for SPT were not found at the subsequent EGD, EMR was therefore not performed. Synchronous SPT was highly suspected in 10 patients. SPT was pathologically confirmed in 6/10 patients. In two of these six patients, radiotherapy field was extended to the esophagus, because of the presence of lymphovascular invasion after endoscopic submucosal dissection (ESD) for T1a ESCC in one patient and T2 ESCC in the other. Four patients had high grade dysplasia or mucosal cancer without adverse criteria, treated with EMR (n=1) or ESD (n=3). In 3/10 patients low grade dysplasia was pathologically confirmed, two were treated with EMR and one patient died due to HNSCC before EMR. In the remaining patient biopsy was not performed to avoid submucosal fibrosis, which might make ESD more difficult. In this patient, ESD and histopathological examination will follow after HNSCC treatment. Of 26 lesions suspected for SPT, six are confirmed SPT, three are confirmed low grade dysplasia, histopathological examination will follow after ESD of one lesion, and no SPT was detected in 16 lesions.

Conclusion: Incidence of synchronous esophageal SPT was 6.5% in our cohort of Western HNSCC patients. Most SPTs were detected in an endoscopic curable stage. This SPT incidence is lower than the incidence found in Asian studies.

Disclosure: Nothing to disclose

P0153

LONG-TERM CLINICAL OUTCOMES AFTER NON-CURATIVE ENDOSCOPIC RESECTION FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Recently, endoscopic resection (ER) is performed for early esophageal squamous cell carcinoma (ESCC) world widely. The additional surgical resection or chemoradiotherapy (CRT) were recommended for the patients with pathological non-curative resection after ER. However, the long-term clinical outcomes after non-curative resection according to the additional treatments were unknown.

Aims & Methods: The aim of this study was to clarify the long-term clinical outcomes after non-curative endoscopic resection for ESCC according to the additional treatments. We retrospectively enrolled patients who treated with ER for ESCC between January 2009 and December 2017 and diagnosed pathologically as invading into muscularis mucosae (MM) in-

volving lymphovascular invasion (LVI) or invading into submucosa (SM), and negative for vertical margin. The patients who had the previous treatment for ESCC except curative ER, finally diagnosed as pMM or shallower invasion without LVI, and those who had synchronous or metachronous multiple cancers within the previous 5 years except Stage I were excluded. The enrolled patients were recommended the additional surgery and CRT, and the following treatment or observation was selected. Surgical method was thoracoscopic or open esophagectomy with D3 lymphadenectomy, and CRT consisted of CDDP (70 mg/m²/day, days 1 and 29) and FU (700 mg/m²/day, days 1-4 and 29-32, civ) with concurrent radiotherapy (41.4 Gy/23 fr). After the additional treatment, upper gastrointestinal endoscopy and computed tomography of the neck, chest, and abdomen were basically performed for every 6 months to evaluate the recurrence. We evaluated the cumulative recurrence rate (CRR), progression-free survival (PFS), and overall survival (OS), and accessed them according to the additional treatment. Lymph node and/or distant recurrence were included events in CRR. This study was approved by an institutional review board in our institution.

Results: Totally, we evaluated the eligible 93 patients, consisted of 72 male and 21 female with median age of 70 years (range 46-88). Endoscopic mucosal resection and endoscopic submucosal dissection was performed in 9 and 84 patients. As the pathological findings after ER, the numbers of patients having pMM with LVI, pSM1 without LVI, pSM1 with LVI, pSM2 without LVI, and pSM2 with LVI were 15/9/7/34/28. Twenty-five patients were observed without any additional treatment, 18 were performed with surgery, and 50 were treated with CRT as the additional treatment. During the median follow-up of 51 months (range 1-123 months), locoregional lymph node recurrences occurred without distant recurrence in 4 patients of observation group and 2 of surgery group. No patients in CRT group developed recurrence. The pathological finding after ER in patients with recurrences were pMM with LVI in one patient, pSM2 without LVI in 2, and pSM2 with LVI in 1 of observation group, and pSM1 with LVI in 2 patients of surgery group. The 3-year CRR, PFS, and OS according to the additional treatment were 9.1%, 81.7%, and 85.4% in observation group, 5.6%, 94.4%, and 94.4% in surgery group, and 0.0%, 98.0%, and 98.0% in CRT group. Of six patients with recurrences, 3 had recurrences more than 4 years later from ER.

Conclusion: Additional treatments showed the better long-term outcomes than observation for patients with non-curative endoscopic resection. As recurrence sometimes occur more than 4 years later from ER even if additional treatment was performed, careful long-term follow up is needed for non-curative resection.

Disclosure: Nothing to disclose

P0154

ENDOSCOPIC FOLLOW-UP OF RADICALLY RESECTED HIGH-RISK MUCOSAL ADENOCARCINOMA AND LOW- AND HIGH-RISK SUBMUCOSAL ADENOCARCINOMA ARISING IN BARRETT'S ESOPHAGUS, RESULTS OF 120 PATIENTS FROM THE DUTCH BARRETT EXPERT CENTER COHORT

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Introduction: After radical endoscopic resection (ER) of an esophageal adenocarcinoma (EAC) in Barrett's esophagus with high risk features, optimal management is unclear. This concerns three groups: high-risk (HR) mucosal (T1a) EAC (poorly (G3)/undifferentiated (G4) cancer a/o lymphovascular invasion (LV+)); low-risk (LR) submucosal (T1b) EAC (submucosal invasion < 500um, well/moderate differentiation, LV-); HR-T1b EAC (invasion >500um, G3/4 cancer a/o LV+). Endoscopic follow-up (FU) to detect lymph node metastases (N+) at a curable stage is considered an option in selected cases, however, optimal FU strategy is unclear. Aim was to evaluate outcomes of endoscopic FU in all patients treated by radical ER for HR-T1a EAC or LR/HR-T1b EAC.

Aims & Methods: Endoscopic therapy for Barrett's neoplasia in the Netherlands is centralized in 9 expert centers with specifically trained endoscopists and pathologists. As part of an ongoing registry, treatment and FU data of all patients treated endoscopically for BE neoplasia in the Netherlands, is collected in a dedicated database. We identified all patients who underwent histologically radical ER for HR-T1a EAC or LR/HR-T1b EAC, followed by endoscopic FU. The decision to follow-up was a shared decision by both patients and the treating physician. Endoscopic FU consisted of gastroduodenoscopy (GDS) ± endoscopic ultrasound (EUS), frequency was determined by the treating physician. Outcome parameters were number of patients with N+, distant metastases (M+) and tumor related death.

Results: From Jan 2008 to Oct 2019, 120 patients (median age 74yrs) underwent radical ER of HR-T1a (n=27), LR-T1b (n=55) or HR-T1b EAC (n=38) and endoscopic FU (median 29 months (IQR 15-48) (see table). Nine patients were diagnosed with N+ (n=4; 3%) and N+M+ (n=5; 4%) after median FU of 27 months (IQR 23-38), of which 6/9 had HR-T1a EAC. N+/M+ was diagnosed by EUS-FNA (n=5), or CT performed for symptoms (n=4). The annual N+/M+ risk was 6,7% in HR-T1a, 0,7% in LR-T1b and 2,1% in HR-T1b patients per year; 4/9 patients with N+ disease were additionally treated with curative intent, of which 1 was cured, 1 is still treated, 2 died of complications. Six patients (5%) died from EAC (of which 2/6 from treatment complications). Non-EAC related mortality was 8,3%.

Conclusion: High-risk mucosal EAC with poor differentiation or lymphovascular invasion was associated with an unexpected high risk of lymph node metastases. The risk for LR-T1b patients was low. In patients diagnosed with N+ during follow-up, treatment with curative intent was still an

option in almost half of patients, and tumor related death was lower than non-tumor related death. Thus, in selected patients with high risk and/or T1b EAC, endoscopic follow-up may be justified, yet the optimal FU regimen to detect N+ at a curable stage is yet to be established.

Disclosure: Nothing to disclose

N=120	Follow-up, months Median (IQR)	Number of GDS, Median (IQR)	Number of EUS, Median (IQR)	N+ / M+ during FU, N (%)	Annual risk N+/M+ during FU (95% CI)	Time to N+, M+, months Median (IQR)	Tumor related death, N (%)	Background mortality (non-EAC related death), N (%)
HR-T1a (n=27)	31 (21-49)	6 (3-8)	1 (0-4)	6 (22%)	6,7% (3-15)	29 (19-52)	4 (15%)	2 (7%)
LR-T1b (n=55)	30 (16-48)	4 (2-7)	1 (0-3)	1 (2%)	0,7% (0-4)	22 (NA)	1 (2%)	6 (11%)
HR-T1b (n=38)	23 (13-52)	5 (3-8)	5 (2-7)	2 (5%)	2,1% (0-7)	29 (NA)	1 (2,5%)	2 (5%)

[Follow-up summary per risk group]

P0155 WITHDRAWN

P0156

ORGAN PRESERVATION AFTER ENDOSCOPIC RESECTION OF EARLY ESOPHAGEAL CANCER WITH A HIGH RISK OF LYMPH NODE INVOLVEMENT

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Introduction: Esophagectomy is recommended after endoscopic resection of an early esophageal cancer in case of pejorative histoprognostic criteria indicating a high risk of lymph node involvement. Our aim was to analyze the clinical outcomes of a non-surgical, organ preserving management in this clinical setting.

Aims & Methods: This retrospective study was performed in two tertiary centers from 2015 to 2019. Patients were included if they had a histologically complete resection of an early esophageal cancer, with, poor differentiation, lymphovascular invasion or deep submucosal invasion. The endoscopic resection was followed by chemoradiotherapy or follow-up in case of surgical contraindications or patient refusal. Outcome measures were the disease-free survival (DFS), overall survival (OS), cancer specific survival (CSS), and the toxicity of chemoradiotherapy.

Results: Forty-one patients (36 with squamous cell carcinomas and 5 with adenocarcinomas) were included. Criteria for non-curative resection were: poor differentiation (n=10), lympho-vascular invasion (n=11), muscularis mucosa invasion (for 5 cases of squamous cell carcinoma) or deep sub-mucosal invasion (n=29). Thirteen patients (32%) were closely monitored, and 20 (49%) and 8 (20%) patients were treated by chemoradiotherapy and radiotherapy alone, respectively. Disease-free survival, overall survival and cancer specific survival were 80.5%, 83% and 98% re-

spectively. In the close follow-up group, disease-free, overall and cancer specific survival were 92%, 92% and 100%, respectively, with a median follow-up of 12 months. In the chemo-radiotherapy group, disease-free, overall and cancer specific survival were 75%, 79% and 96%, respectively, with a median follow-up of 28 months. There was no significant difference between the 2 groups in disease-free survival rate at 1 and 2 years. Serious adverse events related to chemo-radiotherapy occurred in 10% of the patients. There were no treatment-related deaths.

Conclusion: Our study shows that close follow-up could be an alternative to systematic esophagectomy after the endoscopic resection of an early esophageal cancer with a predicted high risk of lymph node involvement.

Disclosure: Nothing to disclose

P0157

TOLERABILITY OF A NON-ENDOSCOPIC DISTAL ESOPHAGEAL SAMPLING DEVICE

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Introduction: Esocheck (Lucid Diagnostics) is an office based, non-endoscopic balloon device for detecting Barrett's esophagus (BE) and esophageal adenocarcinoma (EAC). A two-institution pilot study (PMID: 29343623) demonstrated that a two-marker methylated DNA biomarker panel coupled with the device detected BE/EAC with >90% accuracy. A new improved version (Esocheck) is being tested at 8 tertiary care centers, with procedures performed mostly by non-physicians.

Aims & Methods: To assess the tolerability, swallowability, and safety of Esocheck in this multi-institutional research study.

Research teams (RN Research coordinators and MDs) were trained through watching a video and performing between 2 and 5 supervised procedures prior to performing the Esocheck test independently. Patient differences between those who successfully swallowed the device and those who were unable to were calculated using t-tests and chi-square tests. Logistic regression was performed to determine which factors played a significant role in successful swallowing.

Results: Between March 2018 and November 2019, a total of 406 patients were approached. Of these, ~84% swallowed the device successfully. The mean age of those who succeeded was significantly higher than those unable to swallow the device (60 vs 55 years, p - value 0.007). Patients who could not swallow were significantly more anxious than those who could. The majority were males, white, and were either overweight or obese (Table 1). The majority who successfully swallowed the sampling device did so the first time and required no local anesthetic spray. The type of provider, (MD or RN) did not affect swallowing. Success in performing the procedure ranged from 68% to 96% among the 9 providers who performed more than 10 procedures. The two providers who had performed more

than 100 procedures had a success rate of over 90%. The procedure was well tolerated, 68% preferred it to EGD, and 80% agreed to repeat testing. Gagging and choking scores were significantly lower in the success group (Table 1). Patients who swallowed the device took an average of 2.64 minutes (SD = 1.46 minutes) to get it to the GE junction. In multinomial logistic regression, no one particular factor significantly influenced swallow success. No major adverse events were noted; Grade 1 abrasion was seen in only 1 patient at EGD (< 1%).

Conclusion: Distal esophageal sampling with Esocheck is well tolerated and preferred over EGD by most patients. Younger anxious adults and those with higher gag have greater difficulty in swallowing the device. Providers who performed more than 100 procedures had higher success suggesting performance improves with experience. Esocheck can be quickly and safely performed by trained allied health professionals in an office-based setting.

Disclosure: Nothing to disclose

P0158

NONPHYSICIAN EXPERIENCE WITH NOVEL BARRETT'S SCREENING DEVICE - DESCRIPTIVE STUDY

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Introduction: Mass endoscopic screening for Barrett's esophagus (BE) and esophageal adenocarcinoma (EAC) with EGD is cost-prohibitive and not evidence based. Esocheck is a simple, novel, non-invasive, low-cost, non-endoscopic office-based screening device that can be easily performed by physicians and non-physicians alike and is currently being tested at 8 tertiary care centers across the United States.

Aims & Methods: To describe the experiences of non-physicians (Research Nurse [RN], Research Coordinator [RC]) who are performing the Esocheck procedure in this multi-institution collaborative study.

Non-physician coordinators at participating centers were trained over 1-2 days by experienced personnel from the central coordinating site prior to study initiation. An internally tested, novel, 7-part, 50 item survey was created at the main coordinating center and distributed to the recruitment centers after coordinators had gained ~12 -15 months of experience with the procedure.

Results: Nine non-physician coordinators (2 RNs, 6 RCs and 1 project manager) returned the completed survey. Non-physician coordinators had performed a median of 20 procedures (range, 7-100 procedures). The median years of practice as RN/RC was 10 years (range, 1-20 years). Three out of 9 survey respondents had prior experience administering a swallowed encapsulated sponge screening device. All 9 found in-person training helpful for both patient recruitment and to perform the Esocheck procedure, while 8 found the training video helpful. Coordinators practiced a median of 3 procedures (range, 2-5 procedures) before they started performing Esocheck independently (Table 1), though they said that they felt comfortable doing the procedure on their own after a median of 5 procedures (range, 3-10 procedures). Five out of 9 showed the Esocheck swallowing video to their patients before the procedure. Encouraging deep breaths, explaining the procedure thoroughly, reassurance, and providing encour-

agement were crucial strategies per RN/RCs to increase procedure success. Performance of procedure in physician office was felt to be easier than doing it in endoscopy suite just prior to EGD.Coordinators used a local anesthetic spray (in the form of a spray or gargle) to decrease gag and enable swallowing. Most RN/RCs said they offered the pharyngeal anesthetic to patients on the 2nd try, whereas one coordinator said they would offer it to their patients only on the 3rd try. Coordinator perceptions of patient factors affecting Esocheck swallowing ability are described in Table 2.

Table 1: Survey responses by non-physician coordinators on their training, preparedness, and level of comfort in performing the Esocheck procedure	Median (Range)	Table 2: Non-physician coordinator perceptions of patient factors possibly affecting Esocheck swallowing ability	Median (Range)
Level of preparedness after training to recruit patients	4 (3-5)	Perceived level of anxiety experienced prior and during the procedure	5 (2-7)
Value of Esocheck training video	4 (2-5)	Perceived level of pain experience during the procedure	1 (1-4)
Usefulness of practicing in front of a trainer	5 (3-5)	Perceived level of gagging experienced during the procedure	6 (4-8)
Number of times practiced before performing Esocheck independently	3 (2-5)	Perceived level of choking experienced during the procedure	2 (1-7)
Comfort level at the time of first independently performed Esocheck procedure	3 (2-5)	Perceived overall tolerability of Esocheck procedure	5 (3-7)
Comfort level with independently performing Esocheck at the time of returning survey	5 (4-5)		
Overall preparedness after training to independently perform Esocheck procedure	4 (3-5)		
Number of procedures before coordinator became comfortable performing Esocheck	5 (4-10)		
Reported on a 5-point likert scale, with higher scores being better		Reported on a 10-point likert scale, with higher scores indicating worse tolerability	

[Study Tables]

Conclusion: Non-physicians can be easily trained to perform distal esophageal sampling with the Esocheck device. Non-physicians quickly become comfortable in the procedure and prefer to perform it in an office-based setting often with the aid of a pharyngeal anesthetic.

Disclosure: Nothing to disclose

P0159 WITHDRAWN

P0160

MINIMALLY INVASIVE ESOPHAGECTOMIES ARE MORE BENEFICIAL IN THE TREATMENT OF ESOPHAGEAL CANCER THAN OPEN SURGICAL TECHNIQUES: A NETWORK META-ANALYSIS

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Introduction: Minimally invasive surgical techniques are becoming predominant in all fields of surgery, including oesophageal surgery. Several meta-analyses tried to compare minimally invasive modalities with open techniques, including all types of comparative studies with significant limitations.

Aims & Methods: Our goal is to compare all surgical modalities to each other from results of randomized controlled trials, thus providing objective evidence and a ranking of the different techniques regarding survival, complication rate, operation time, hospital stay, and blood loss. We conducted a systematic search of the PubMed, Embase, and Cochrane databases to identify relevant studies and performed a network meta-analysis (NMA). We used the random effect model. To ensure the interpretability of the NMA results, we will present the geometry of the network, the results with probabilistic statements, and estimates of interventions' effects along with their corresponding 95 % credible interval (CI), as well as forest plots. For ranking the interventions, we chose to use the surface under the cumulative ranking (SUCRA) curve, which provides a numerical summary of the rank distribution of each treatment.

Results: We included 12 studies in our analysis. A significant difference was found considering pulmonary infection, which favored the laparoscopic intervention compared to transthoracic surgery (risk ratio 0.49, 95% credible interval 0.23 to 0.99). Operation time was significantly shorter for transhiatal approach compared to transthoracic surgery (mean difference -85 minutes, 95% credible interval -150 to -29), hybrid intervention (mean difference -98 minutes, 95% credible interval -190 to -9.4), laparoscopic technique (mean difference -130 minutes, 95% credible interval -210 to -50), and robot-assisted esophagectomy (mean difference -150 minutes, 95% credible interval -240 to -53). Other comparisons did not yield significant differences.

Conclusion: While individual studies suggest the superiority of the minimally invasive techniques regarding multiple outcomes, the summarized evidence is only conclusive considering the complication rate and operation time. Although the tendency suggests that minimally invasive techniques have better results, more randomized controlled trials are needed to achieve statistical significance and more definite evidence.

Disclosure: Nothing to disclose

P0161

LONG-TERM FOLLOW-UP AFTER NON-CURATIVE SUPERFICIAL SCC ENDOSCOPIC RESECTION WITH ADJUVANT TREATMENT: A MULTICENTER WESTERN STUDY

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Introduction: In case of non-curative endoscopic resection of superficial esophageal squamous cell carcinoma (SCC), adjuvant treatment by chemoradiotherapy (CRT) can be an alternative to surgery.

Aims & Methods: The aim of this study was to assess long-term clinical and oncological outcomes in patients treated with adjuvant CRT or not, after non-curative superficial SCC endoscopic resection. We conducted a retrospective multicenter study in eleven French tertiary care hospitals. Patients treated by endoscopic resection for histologically proven SCC with tumor depth infiltration deeper than the muscularis mucosae were included consecutively. High risk of nodal or/and distal metastasis was defined by tumors with infiltration depth in Sm >200 µm, or positive lymphovascular invasion, or mild and poor differentiation.

Results: 137 endoscopic resections in 132 patients were analyzed. The nodal or distal metastasis recurrence-free survival rate at 5 years was 88%. The death-free survival rate at 5 years was 60.3% for all causes, and 86% due to esophageal cancer. Risk of metastasis strongly increased in patients without adjuvant treatment ($P = 0.01$). Independent factors for nodal or/and distal metastasis cancer recurrence were age ($HR = 1.075$ (95% CI: 1.007-1.149, $P = 0.031$), tumor infiltration depth in Sm >200 µm, $HR = 4.129$ (95% CI: 1.067-15.977, $P = 0.040$), and no adjuvant treatment by CRT or surgery $HR = 11.322$ (95% CI: 1.281-100.033, $P = 0.029$). High risk of nodal involvement or metastasis was found in 83 tumors (60.6%), and adjuvant therapy reduced the risk of recurrence ($p = 0.008$). The nodal and distal metastasis recurrence-free survival rate at 5 years was 100% after adjuvant surgery and 97.1% for CRT ($P = 0.542$).

Conclusion: Combination therapy with endoscopic resection followed by adjuvant CRT reduce the risk of nodal recurrence. This strategy should be considered as an alternative to surgery for patients with severe comorbidities treated endoscopically for superficial SCC with a high risk of lymph node invasion.

Disclosure: Nothing to disclose

P0162

A NOVEL APPROACH TO RADIOTHERAPY TARGETING FOR OESOPHAGEAL SQUAMOUS CELL CANCER USING LUGOL'S IODINE GUIDED ENDOCLIP MARKING

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Introduction: Squamous cell carcinoma (SCC) of the oesophagus often presents at a late stage with dysphagia symptoms. Chemoradiation (definitive or neoadjuvant treatment) remains the standard strategy for the treatment of localised SCC. Accurate radiotherapy target delineation is however problematic for very early tumours that cannot be visualised on cross-sectional imaging. We describe a novel technique of endoscopic clip placement to mark the area for targeted radiotherapy, in conjunction with Lugol's iodine chromoendoscopy to delineate the dysplastic field.

Aims & Methods: We aimed to evaluate outcomes in patients receiving Lugol's iodine chromoendoscopy guided clip deployment to mark radiotherapy field in a tertiary centre. A prospective study of procedures performed using the technique between 2017 and 2020 was undertaken. Unstained lesions (USL) were described and photographed. The proximal and distal extent of USLs were marked with ResolutionTM endoclips (Boston Scientific) which were placed on normal appearing squamous tissue 0.5cm away from the USL. Four operators carried out the procedures with expertise in Endoscopic Eradication therapy and lesion recognition. Endoscopy reports, clinic letters, and imaging modalities were all interrogated to evaluate patient outcomes.

Results: Fifteen patients were enrolled, 4 male, 11 female. Thirteen (86.7%) were for a new diagnosis of SCC, and 2 (13.3%) were for SCC recurrence. All patients were staged as T2N0M0 on CT. Eight patients had prior EUS and 13 had PET-CT scans, but these imaging modalities could only detect the area of abnormality in 3 (20%), and 4 (26.7%) of cases respectively. Lugol's Chromoendoscopy was able to clearly delineate the dysplasia in all cases (100%). The mean total length of oesophageal USL marked with clips was 7.3 cm +/- 3.8. The mean length of endoscopic procedure was 9.2 minutes +/- 2.4. All procedures were undertaken with conscious sedation with a median dose of 2.5mg midazolam (2.5-3.0) and 50mcg fentanyl (0-75mcg). All 15 patients scored comfortable on a GRS scale. Mean time from clip deployment to CT radiotherapy planning scan was 7.8 days (+/- 5.1). No clips fell off prematurely requiring repeat endoscopy. Median dose of radiotherapy delivered was 50Gy. At 12-months, of those followed up 26.7% had evidence of relapse free survival.

Conclusion: Here we describe a novel technique using Lugol's guided clip placement prior to radiotherapy, demonstrating it to be a quick and uncomplicated procedure which can be used in the management of patients with SCC.

Disclosure: Nothing to disclose

P0163

ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OF SQUAMOUS NEOPLASIA OF THE OESOPHAGUS IN THE WEST - A MULTICENTRE EUROPEAN STUDY

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Introduction: The management of squamous cell neoplasia of the oesophagus has been revolutionised by the adoption of endoscopic submucosal dissection (ESD). The Japanese Oesophageal Society cancer practice guidelines currently recommend that radical endoscopic treatment can be considered for intra-mucosal lesions confined to the epithelium or lamina propria (pT1a M1 or M2). The reported risk of lymph node metastasis in neoplasia with invasion deeper than M2 is considered unacceptably high and non-curative, however the risk of radical surgery or chemoradiotherapy is not insignificant, especially in an ageing Western population. It is also noteworthy that ESD of squamous oesophageal neoplasia is not as common in the West as it is in the East, as it is considered as a very high risk procedure.

Aims & Methods: Our aim was to evaluate the outcome of ESD for squamous neoplasia of the oesophagus in the hands of Western endoscopists. We performed a retrospective analysis of all oesophageal squamous ESDs performed across 4 tertiary referral centres in Europe (UK, Switzerland, Poland, Italy) between 2011-2020. The primary outcome was sole endoscopic management at 1 year post resection.

Results: 89 squamous ESDs were performed in 81 patients. The mean age was 67 years with 60% being male. Average lesion size was 37mm (range 10-110mm) and commonest location was mid-oesophagus. The en-bloc resection rate was 98%. There were 2 perforations (1 surgery, 1 stent), 1 delayed bleed (managed with blood transfusion) and 25 post-procedural strictures (all managed with dilatation or stent). The R0 resection rate was 95% in lesions ≤M2 and 82% in lesions >M2 (p<0.001).

1 year follow up data was available on 64 patients (see table 1). 32/34 (94.1%) of patients meeting curative resection criteria achieved endoscopic only management at 1 year. This dropped down to 23/30 (76.7%) in those with non-curative resection. Recurrence or metachronous lesions were found in 6 of the curative group and 2 of the non-curative group (all treated endoscopically). 1 patient in the non-curative group developed lymph node metastasis.

Group n = 64	Surgery (n, %)	Chemoradiotherapy (n, %)	Died (n, %)	Recurrence or metachronous lesion (n, %)	Dysplasia free endoscopic follow up (n, %)
≤M2 (n=34)	1 (2.9)	0 (0)	1 (2.9)	6 (17.6)	26 (76.5)
>M2 (n=30)	3 (10.0)	4 (13.3)	0 (0)	3 (10.0)	20 (66.7)

[Table 1 - Patient status at 1 year post resection in curative (≤M2) vs non-curative resection group (>M2)]

Conclusion: Our data demonstrates that although the overall numbers of ESD for squamous neoplasia carried out in a Western setting are limited, the complication rates are low and most are managed endoscopically. Almost half of the patients had advanced disease, but this did not increase

the complication rates. The overall outcome in those with non curative resection was technically not much different, raising a possibility to consider ESD as a radical treatment for those who are otherwise not fit for surgery or chemoradiotherapy.

Disclosure: Nothing to disclose

P0164

BISPHOSPHONATE TREATMENT OF OSTEOPOROSIS DOES NOT INCREASE THE RISK OF SEVERE GASTROINTESTINAL SIDE EFFECTS: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Bisphosphonates (BPs) are first-line therapy for severe osteoporosis. BPs-related gastrointestinal (GI) adverse events are primarily responsible for low adherence. Bisphosphonates appear to be effective, however this topic remained conflicting because of the inconsistent results from the studies available so far.

Aims & Methods: Our meta-analysis aims to objectify the risk of severe GI adverse events due to BP therapy in osteoporotic patients.

A systematic search was conducted in three databases up to July 2019 for randomized controlled trials (RCTs) detailing gastrointestinal adverse events in adult patients with osteoporosis on the BP and placebo arms. Risk ratios (RRs) 95% with confidence intervals (CI) were calculated for non-severe and severe adverse events with the random-effects model. Statistical heterogeneity was assessed using chi² and I² statistics.

Results: Forty-two RCTs with 39,335 patients with 9,999 non-severe and 1,503 severe GI adverse events were included. The incidence of non-severe and severe adverse events ranged between 0.3-54.9% and 0-10.3%, respectively. There was no difference between BP and control groups in terms of the risk of non-severe or severe side effects: RR=1.05 (CI: 0.98 - 1.12), I²=48.1%, and RR=1.01 (CI: 0.92 - 1.12), I²=0.0%, respectively. Subgroup analysis of the most commonly used BP, once-weekly alendronate 70 mg, revealed no association between bisphosphonates and the risk of non-severe and severe GI adverse events [RR=1.16 (CI: 1.00 - 1.36), I²=40.7% and RR=1.20 (CI: 0.83 - 1.74), I²=0.0%].

Conclusion: Our results show that bisphosphonates do not increase the risk of severe GI adverse events, requiring specialist care or endoscopy. However, the marked variability of the screening for side effects in included studies limits the strength of evidence of our result.

Disclosure: Nothing to disclose

P0165

NOVEL METAL-FREE CARBON MONOXIDE-RELEASING PRODRUG IN PREVENTION OF GASTRIC MUCOSA AGAINST NSAIDS-INDUCED GASTROTOXICITY

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Introduction: Carbon monoxide (CO) is produced endogenously in GI tract by the activity of heme oxygenase (HMOX). Additionally, CO-releasing pharmacological tools have been shown in experimental studies to exert anti-inflammatory and anti-oxidative properties maintaining gastric mucosal integrity. But the clinical implementation of these compounds is debatable due to the presence of metals in their chemical structure. We aimed to assess the effectiveness of our novel metal-free CO-based therapeutic, BW-CO-111 administered i.g. against the development of aspirin-induced GI damage.

Aims & Methods: Wistar rats were pretreated with vehicle or BW-CO-111 (0.02-5 mg/kg i.g.) or BW-CP-111, the product after CO release from BW-CO-111. After 30 min, gastrotoxicity was induced by administration of aspirin (125 mg/kg i.g.). Gastric damage area and gastric blood flow (GBF) was determined by planimetry, histology and laser flowmetry, respectively. Gastric mucosal mRNA and/or protein expressions of HMOX-1, HMOX-2, Nrf-2, COX-1, COX-2, iNOS, annexin-A1 and TGF-β1 as well as serum contents of TGF-β1, TGF-β2, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12, TNF-α, IFN-γ, and GM-CSF were determined by real-time PCR, Western blot or Luminex platform, respectively. CO content in gastric mucosa was assessed by gas chromatography. Gastric mucosal PGE₂ content was determined by ELISA.

Results: Pretreatment with BW-CO-111 (0.1 mg/kg i.g.) increased gastric mucosal content of CO and reduced gastric damage area accompanied by an increased GBF. CO-prodrug decreased and upregulated gastric mucosal mRNA expression for pro-inflammatory iNOS and anti-inflammatory annexin-A1, respectively. BW-CO-111 maintained increased by aspirin serum content of anti-inflammatory TGF-β1 and -β2 but did not affect systemic inflammatory response and PGE₂ content alterations in gastric mucosa induced by aspirin. BW-CP-111 did not affect gastric mucosal integrity and molecular pathways expression.

Conclusion: We conclude that BW-CO-111 applied i.g. protected gastric mucosa against aspirin-induced damage due to its ability to release CO, responsible for the gastric microcirculation increase and due to the activation of molecular anti-inflammatory response within gastric mucosa. This novel metal-free CO-prodrug seems to be promising compound for the further development of safer clinical GI pharmacology.

Disclosure: [This study has been partly supported by National Science Centre in Poland (grant no: UMO-2019/33/B/NZ4/00616)]

P0166

PROTECTIVE EFFECT OF PPI AGAINST GASTRIC MUCOSAL INJURIES IN PATIENTS TAKING EACH DOACS - COMPARISON AMONG INDIVIDUAL DOACS

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Introduction: It has been known that bioavailability and activation rate of drugs in the gastrointestinal tract are very different among individual direct oral anticoagulants (DOACs)⁽¹⁾. Therefore, as in the case of the upper gastrointestinal (GI) bleeding risk, the prevalence of gastric mucosal injury is considered to be different among individual DOACs⁽²⁾. Since GI bleeding risk can be reduced by concomitant use of proton pump inhibitor (PPI)⁽³⁾, we recently reported that concomitant use of PPI reduces the prevalence of gastric mucosal injury in DOACs users⁽⁴⁾. As in previous studies, it is not difficult to image that the effect of PPI to the gastric mucosal injury can be different among individual DOACs.

Aims & Methods: The aim of this study is to explore whether PPI play a protective role for gastric mucosa in patients taking each DOACs (Dabigatran, Edoxaban, Rivaroxaban, Apixaban) or VKA (Warfarin). To reveal the role of PPI, we compared the severity of gastric mucosal injury between PPI users and no antacid users in the subjects taking each DOACs or VKA, individually. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2015 and June 2019. Of the 5,293 subjects analyzed, we focused on 270 subjects who took DOACs or VKA. After excluding subjects who took other type of antacid (histamine 2 receptor blockers or potassium competitive acid blockers), we divided subjects into two subgroups: anticoagulant use with PPI (PPI group), or anticoagulant use without any antacids (no antacid group). Severity of gastric mucosal injury was evaluated endoscopically according to the modified LANZA score (MLS). Statistical analyses were performed by Fisher's exact test.

Results: This study included 101 subjects in PPI group (Dabigatran 12, Edoxaban 18, Rivaroxaban 19, Apixaban 18, Warfarin 34) and 143 subjects in no antacid group (D 20, E 17, R 26, A 21, W 59). In PPI group, average MLS were D: 0.50±1.10, E: 0.41±1.06, R: 0.46±0.95, A: 0.43±0.96 and W: 0.56±1.29, respectively. In no antacid group, average MLS were D: 1.42±1.68, E: 1.06±1.76, R: 0.84±1.42, A: 1.33±1.53 and W: 1.71±2.10, respectively. There was no significant difference of MLS among individual DOACs and VKA in both groups. In the subjects taking Apixaban and warfarin, MLS was significantly lower in PPI group than in no antacid group. However, in the subjects taking Dabigatran, Edoxaban and Rivaroxaban, MLS was tended to be lower in PPI group than in no antacid group but the difference was not significant.

Conclusion: PPI play a protective role in gastric mucosa in patients taking each DOACs, especially in the case of taking Apixaban.

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Disclosure: Nothing to disclose

P0167 WITHDRAWN

P0168

PREDICTIVE SIGNIFICANCE OF ENDOSONOGRAPHIC (EUS) STAGING IN LOCALLY ADVANCED GASTRIC (GC) OR GASTROESOPHAGEAL-JUNCTION (AEG) ADENOCARCINOMA: ANALYSIS OF DATA FROM A PERIOPERATIVE AIO-CAO PHASE II STUDY

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Introduction: This AIO-CAO Phase II Study investigated the additional administration of Panitumumab to a basic ECX therapy (Epirubicin, Cisplatin and Capecitabine) in GC or AEG. This evaluation correlated the preoperative EUS, after neoadjuvant chemotherapy, with the therapy response in addition to the initial examination (baseline EUS).

Aims & Methods: 160 patients from 22 German centers were included. Preoperative uT/uN stages were compared with histopathological pT/pN stages. Each reduction in the T-stage from preoperative EUS to baseline EUS was evaluated as downstaging (DS+) and compared with histopathological regression (grade 1-2 according to Becker) as well as overall survival (OS) of the patient without downstaging (DS-). The preoperative N-stage (positive N+ or negative N-) was correlated with OS too.

Results: In 48% the preoperative EUS T-stage correlated with the pT-stage (sensitivity 48%, specificity 52%) and in 64% the preoperative EUS-N stage correlated with the pN-stage (sensitivity 76%, specificity 52%). With DS+, a tendency towards improved OS was detectable (median OS DS+: median OS not reached during observation time (NA), median OS DS-: 38.5 months (M), p=0.18). The OS of the N+ patient (median OS 36.1 M, p = 0.0045) was worse in comparison to the N- patient (median OS NA).

Conclusion: Despite multicenter participation and different EUS devices, this large prospective study showed a restricted diagnostic accuracy (DA) of preoperative EUS, especially in comparison to DA of initial EUS described in prior studies. The preoperative positive EUS-N status is predictive for a worse prognosis.

Therefore, an alternative procedure should be discussed and evaluated in further studies to improve the OS of the subgroup of these patients.

Disclosure: Nothing to disclose

P0169 WITHDRAWN

P0170 WITHDRAWN

P0171

PLATELET AGGREGATION TEST IN PATIENTS WHO RECEIVED GASTRIC ESD UNDER CONTINUOUS ANTIPLATELET AGENTS

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Introduction: Bleeding after endoscopic submucosal dissection (ESD) is the most frequent adverse event. Several reports showed that taking antiplatelet agents increase the risk of post-ESD bleeding, especially in the cases of taking thienopyridine or dual antiplatelet therapy. Recently, platelet aggregation test is performed for the assessment of secondary prevention of ischemic heart disease and cerebrovascular disorders, but there is no report on this test for evaluating the risk of post-ESD bleeding taking antiplatelet agents. Therefore, we performed platelet aggregation test in patients who received gastric ESD under continuous antiplatelet agents in our hospital to reveal the relationship between patient characteristics and the levels of platelet aggregometry.

Aims & Methods: Between April 2013 and March 2019, a total of 75 cases were performed gastric ESD and assessed by the aggregometer (PRP313 M, TAIYO Inc.) before procedures under continuous antiplatelet agents such as thienopyridine, aspirin, or cilostazol. Five patients taking anticoagulant agent or only other antiplatelet agent were excluded from this study. Finally, 70 cases were enrolled in this study. Platelet aggregation level was compared according to the grading types (G-type) classified by aggregometer. We retrospectively evaluated the relationship between the platelet aggregation level and the patient characteristics such as age, sex, drugs, comorbidities, the duration and curative rate of the procedure, and the incidence of complications.

Results: The study subjects were 47 men and 23 women at a median age of 79 years (range, 64 - 90 years). Patients taking thienopyridine, aspirin, or cilostazol were 17 cases, 36 cases, 20 cases, respectively, and patients taking dual antiplatelet therapy were 10 cases. En-bloc resection was achieved in all cases with median procedure duration of 70.5 min (25-195 min), and curative resection was achieved in 67 cases. There was no perforation case in this study, but post-ESD bleeding occurred in 8 cases.

Median G-type was -1 for the taking thienopyridine group and 0 for the taking no thienopyridine group, and there was a significant difference in the two groups (p = 0.0036). G-type was also significantly lower in the dual antiplatelet therapy group than in the single antiplatelet therapy group (p=0.0031). The median G-type in post-ESD bleeding cases was lower than that in no bleeding cases, but it was not significant (p=0.075).

Conclusion: The levels of platelet aggregometry is low in the cases taking thienopyridine or dual antiplatelet therapy, and the risk of post-ESD bleeding in patients under continuous antiplatelet agents might be assessed by platelet aggregation test.

Disclosure: Nothing to disclose

P0172 WITHDRAWN**P0173 WITHDRAWN****P0174****GASTRIC ADENOCARCINOMA OF FUNDIC-GLAND DIFFERENTIATION**

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Introduction: We previously proposed gastric adenocarcinoma of fundic-gland type (GA-FG) as a new form of gastric adenocarcinoma with distinct clinicopathological and endoscopic features [1-4]. GA-FG was newly added as a special type cancer in Japanese classification of gastric carcinoma, the 15th Edition, 2017, and also listed as a new and rare gastric neoplasia in WHO Classification of Tumours, 2019. Recently, some cases of an aggressive variant of GA-FG with high cellular atypia have been discovered. This variant exhibited differentiation toward gastric foveolar epithelium in addition to fundic gland differentiation, and it was designated gastric adenocarcinoma of fundic gland mucosa type (GA-FGM). Therefore, gastric adenocarcinoma of fundic-gland differentiation (GA-FGD) can be classified into GA-FG and GA-FGM histopathologically. However, the etiology, classification, and clinicopathological features of GA-FGD has not been well elucidated.

Aims & Methods: We performed a large, multicenter, retrospective study to establish a new classification and clarify the clinicopathological features of GA-FGD. A total of 149 GA-FGD lesions were retrospectively collected from 35 institutions during 2008-2019. Of 149 lesions, 100 lesions in 94 patients were enrolled in this study. We designed a new histopathological classification of GA-FGD using an immunohistochemical analysis and compared them clinicopathologically. To establish molecular pathological concept of GA-FGD, next generation sequencing was employed for 34 GA-FGD lesions.

Results: GA-FGD was classified into 2 major types; GA-FG (Type A: intramucosal lesion of GA-FG, n=20 and Type B: submucosal lesion of GA-FG, n=55), and GA-FGM (Type C, n=25). In addition, GA-FGM (Type C) was classified into 3 subtypes; Type C-1 (ordered with exposure type, n=11): the normal architecture or differentiation of fundic gland mucosa (superficial foveolar differentiation and deeper fundic gland differentiation) is preserved, Type C-2 (disordered with exposure type, n=10): its architecture or differentiation is collapsed, and tumor is exposed on the surface, and Type C-3 (disordered with non-exposure type, n=4): its architecture or differentiation is collapsed, and tumor is covered by non-neoplastic mucosa. The average of tumor size (mm, Type A 7.1 vs. Type B 8.4 vs. Type C 20.8, p<0.01) and depth of submucosal invasion (μm, Type B 251.5 vs. Type C 1212.5, p<0.01) were significantly greater in GA-FGM than in GA-FG. Furthermore, the rates of lymphatic and venous invasion and p53 overexpression were significantly higher in GA-FGM than in GA-FG (Ly: 0% vs. 0% vs. 24%, p<0.01, V: 0% vs. 1.8% vs. 20%, p<0.05, p53: 0% vs. 2% vs. 21.1%, p<0.05). The average of tumor size (mm, Type C-1 11.6 vs. Type C-2 31.8 vs. Type C-3 18.5mm, p<0.05) was significantly greater and the rates of lymphatic invasion (0% vs. 60% vs. 0%, p<0.05) was significantly higher in Type C-2 than in Type C-1, C-3. GA-FG had low malignant potential, and

GA-FGM should be categorized as an aggressive variant of GA-FGD that has high malignant potential (Type C-2 > Type C-1, C-3). The frequent presence of GNAS mutation was a characteristic genetic feature of GA-FGD (7/34 20.6%; Type A 1/3 33.3%, Type B 3/24 12.5%, Type C 3/7 42.9%).

Conclusion: We established a new histopathological classification of GA-FGD and proposed a new lineage of gastric adenocarcinoma related to GNAS mutation, and this classification is useful to estimate its malignant potential and establish a standard therapeutic approach for GA-FGD.

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Disclosure: Nothing to disclose

P0175**P53 PROTEIN OVEREXPRESSION IN GASTRIC CANCER ACCORDING TO LAUREN HISTOLOGIC CLASSIFICATION: RETROSPECTIVE STUDY**

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Introduction: p53 gene is a tumor suppressor gene that inactivates in development of malignancies including gastric cancer (GC) through the altered role in cell cycle arrest and induction of apoptosis. Several studies have suggested different results about the relationship between p53 protein overexpression and survival in GC. In addition, the effect of p53 overexpression in two types of Lauren classification has not been known, so far.

Aims & Methods: The aim of this study was to evaluate the prognostic significance of p53 overexpression in GC and the effect on Lauren histology. From May 2003 to December 2019, 3314 patients with GC who were treated with endoscopic or surgical treatment at Seoul national university Bundang hospital were analyzed retrospectively. Immunohistochemical (IHC) analysis for p53 expression was investigated in endoscopic and surgical gastric specimens. Results were analyzed in difference of clinicopathologic characteristics and survival rate according to p53 expression in IHC. Also, subgroup analysis according to Lauren classification was performed.

Results: Among 3314 patients, total 3201 patients were analyzed with IHC stain for presence of p53 protein overexpression. Among 3201 patients, 1175 (36.7%) were p53 protein overexpression positive and 2026 (63.3%) were negative. p53 overexpression was associated with male, presence of atrophic gastritis, intestinal-type, and location of lower third of GC. Other variables including proportion of early GC (EGC) and TNM staging were no significant differences between positive and negative patients. However, in subgroup analysis, p53 overexpression in intestinal-type GC was associated with EGC and lower depth of invasion. In case of diffuse-type GC p53 overexpression was associated with advanced GC (AGC) and advanced TNM stage (Number(proportion) of EGC and AGC, 712:185 (79.4%:20.6%) vs 106:172 (38.1%:61.9%), p-value <0.001, Table).

The overall survival of p53-positive patients was significantly lower than p53-negative patients regardless of histologic subtype. ((A) Total group: p53-negative patients 0.739 vs p53-positive patients 0.626, p <0.001; (B)

Intestinal: 0.714 vs 0.611, $p=0.042$; (C) Diffuse: 0.765 vs 0.642, $p<0.001$; Figure 1.) The cumulative GC specific survival (GC-SS) of p53-positive patients had statistical significance in the diffuse-type gastric cancer patients group and not in other groups ((A) Total 0.874 vs 0.860, $p=0.282$ (B) Intestinal 0.920 vs 0.916, $p=0.775$ (C) Diffuse 0.828 vs 0.737, $p=0.001$, Figure 2.). **Conclusion:** In conclusion, p53 overexpression was associated with EGC in intestinal type contrast to AGC in diffuse type. In addition, p53 overexpression was associated with poor prognosis in GC, especially in diffuse-type patients, suggesting that p53 overexpression plays a different role in the gastric carcinogenesis depending on tissue type.

	Total GC (n=3201,100%)			Intestinal-type GC (n=2100,100%)			Diffuse-type GC (n=1101,100%)		
	p53-(%) (n=2026, 63.3%)	p53+(%) (n=1175, 36.7%)	p-value	p53-(%) (n=1203, 57.3%)	p53+(%) (n=897, 42.7%)	p-value	p53-(%) (n=823, 74.8%)	p53+(%) (n=278, 25.2%)	p-value
EGC vs AGC (EGC)	1406 (69.4)	818 (69.6)	0.905	901 (74.9)	712 (79.4)	0.016	505 (61.4)	106 (38.1)	<0.001
EGC vs AGC (AGC)	620 (30.6)	357 (30.4)		302 (25.1)	185 (20.6)		318 (38.6)	172 (61.9)	
T (T1+T2)	1632 (80.7)	967 (82.8)	0.143	1033 (86)	817 (91.2)	<0.001	599 (72.9)	150 (55.1)	<0.001
T (T3+T4)	391 (19.3)	201 (17.2)		168 (14)	79 (8.8)		223 (27.1)	122 (44.9)	
N (Negative)	1491 (74.9)	859 (74.6)	0.898	969 (81.8)	729 (82.8)	0.561	522 (64.8)	130 (48)	<0.001
N (Positive)	500 (25.1)	292 (25.4)		216 (18.2)	151 (17.2)		284 (35.2)	141 (52)	
M (Negative)	1986 (98.1)	1140 (97.1)	0.085	1189 (98.9)	884 (98.7)	0.685	797 (96.8)	256 (92.1)	0.001
M (Positive)	39 (1.9)	34 (2.9)		13 (1.1)	12 (1.3)		26 (3.2)	22 (7.9)	

[Baseline characteristics of gastric cancer patients in different Lauren subtypes depending on p53 overexpression.]

Data are presented as number (%) or mean.

p-value was calculated using; Chi-square test for categorical variables.

Reference: EGC, Early gastric cancer; AGC, Advanced gastric cancer; GC, Gastric cancer.

Bold style indicates statistical significance.

Disclosure: Nothing to disclose

P0176 WITHDRAWN

P0177

THE METASTATIC PATTERN OF INTESTINAL AND DIFFUSE TYPE GASTRIC CARCINOMA - A DUTCH NATIONAL COHORT STUDY

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Introduction: The Lauren classification of gastric adenocarcinoma describes three histological subtypes, the intestinal, the diffuse and the mixed type carcinoma. The metastatic pattern of gastric adenocarcinoma by histological subtype according to the Lauren classification has not yet been studied.

Aims & Methods: Gastric adenocarcinoma patients with metastatic disease at the time of diagnosis between 1999 and 2017 were identified through the Netherlands Cancer Registry (NCR). The Lauren classification was determined based on pathology reports archived in the Dutch Pathology Registry and was linked to individual cases in the NCR. Differences between histological subtypes were analyzed using the Chi-squared test. Overall survival was calculated with the Kaplan-Meier method and was compared between groups with the log-rank test.

Results: Among 8.140 newly diagnosed, metastatic and evaluable gastric adenocarcinoma patients, 57% had an intestinal type carcinoma, 39% patients had a diffuse type carcinoma and 4% had a mixed type carcinoma. Intestinal type carcinomas more often metastasized to the liver (56% versus 20%, $p<0.001$) and lungs (13% versus 7%, $p<0.001$), whereas diffuse type carcinomas more often metastasized to the peritoneum (58% versus 29%, $p<0.001$) and bones (9% versus 6%, $p<0.001$). (**table 1**) Median overall survival of all patients was 4.1 months and was different for patients with an intestinal type carcinoma than for patients with a diffuse type carcinoma: 4.2 months versus 3.9 months, respectively ($p<0.001$). Location specific survival for patients with metastatic disease at a single location differed by histological subtype (diffuse versus intestinal) for peritoneal (median 4.7 versus 5.0 months, $p=0.002$), liver (median 3.3 versus 3.9 months, $p=0.045$), lung (median 5.0 versus 6.5 months, $p=0.030$) and extra-regional lymph node metastases (median 5.0 versus 8.0 months, $p<0.001$), respectively.

	Total (n=8140)		Intestinal type (n=4632)		Diffuse type (n=3149)		Mixed type (n=359)		p-value
Metastatic location	n	(%)	n	(%)	n	(%)	n	(%)	
Peritoneum	2306	(28)	1335	(29)	1840	(58)	184	(51)	<0.001
Liver	3354	(41)	2613	(56)	641	(20)	100	(28)	<0.001
Lung	847	(10)	583	(13)	228	(7)	36	(10)	<0.001
Extra-regional lymph nodes	3359	(41)	1337	(29)	867	(28)	102	(28)	0.44
Bones	579	(7)	255	(6)	294	(9)	30	(8)	<0.001
Adrenal gland	198	(2)	133	(3)	54	(2)	11	(3)	<0.001
Other	480	(6)	223	(5)	229	(7)	28	(8)	<0.001

[Table 1]

Conclusion: In this national cohort study, metastatic gastric adenocarcinoma of the intestinal type had a predilection for the liver and that of the diffuse type for the peritoneum. As holds true for non-metastatic gastric cancer, patients with an intestinal type tumor have a better survival than patients with a diffuse type tumor.

Disclosure: Nothing to disclose

P0178 WITHDRAWN

P0179

LONG-TERM OUTCOMES AFTER ENDOSCOPIC RESECTION FOR LATE ELDERLY PATIENTS WITH EARLY GASTRIC CANCER

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Introduction: The incidence of gastric cancer (GC) and the death of GC in the elderly patients are increasing in Japan. And endoscopic resection (ER) is more often performed than surgery for GC in Japan. However, there are few reports on the outcomes of elderly patients with gastric cancer after ER. In this study, we examined the long-term outcomes after ER for elderly patients with gastric cancer in our institute.

Aims & Methods: Among 1,353 early GC patients who underwent ER at our hospital from January 2007 to December 2012, 400 patients who were 75 years or older at the time of ER were included. We investigated the patient's survival and the cause of death at 7 years later from the year of ER by medical records of our hospital, the Osaka Cancer Registry, and contact their primary care doctor. We examined the association between patient and lesion characteristics with the overall survival (OS). We used the endoscopic curability (eCura) classifications: eCura A is curative resection, B is expanded curative resection, C-1 is non-curative resection only with piecemeal resection or a positive horizontal margin in histologically differentiated cases, C-2 is non-curative resection excluding C-1 (Japanese Gastric Cancer A. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer. 2020).

Results: 292 men and 108 women with a mean age of 79.3 years (range 75-93 years) were included. The treatment method was endoscopic submucosal dissection (ESD) in 378 cases and endoscopic mucosal resection (EMR) in 22 cases, and the en bloc resection was obtained in 97.5%. Performance Status (PS) was 0 or 1 in 395 cases and 2 to 4 in 5 cases. Prognostic nutritional index (PNI) was 48.4 on average (range 28.7-63.2). Charlson Risk Index (CCI) was 0 or 1 in 229 cases and 2 or more in 171 cases. Pathological diagnosis revealed that the main histologic type was differentiated type in 378 cases and undifferentiated type in 22 cases, 316 were intramucosal cancer, 26 were submucosal cancer with slight invasion, and 58 were submucosal cancer with massive invasion (more than 500 micrometer[SS1] [kw2]), and lymphatic invasion was observed in 33 cases. 284 were eCura A, while 25 were B, 7 were C-1, and 84 were C-2. The prognosis capture rate was 89% at 5 years and the 5-year OS rate was 80.8%. There were 88 deaths and 7 (8%) caused by GC, all of which were eCura:C-2. As a result of the univariate analysis by the log-rank test, "age 79 or more", "PS 2 or more", and "PNI 49 or less" were significant factors with a poor prognosis of OS. Among lesion factors, "lesion size 20mm or more", "undifferentiated type", "SM2 invasion[SS3] ", "vertical margin indeterminate or positive", "lymphatic invasion" and "eCura: C-2" were significant factors with poor prognosis. A multivariate analysis using Cox proportional hazard regression (hazard ratio [95% confidence interval]) for the factors of "age", "PS", "PNI", "CCI", "eCura", and " lymphatic invasion " showed that "PS 2 or more (10.3 [3.14-34.0])", "PNI $\leq$ 49 (2.63 [1.62-4.28])", "eCura C-2 (2.00 [1.26-3.18])" were independent risk factor for poor prognosis of OS.

Conclusion: The factors of poor prognosis of OS after ER for late elderly patients with early GC were "PS 2 or more", "PNI 49 or less", and "eCura C-2" in this study. Although background factors such as PNI and CCI were only associated with the prognosis for elderly patients according to previous reports, we should also take into consideration about additional surgery in case of non-curative resection (eCura C-2).

Disclosure: Nothing to disclose

P0180

HELICOBACTER PYLORI ERADICATION PREVENTS METACHRONOUS GASTRIC CANCER IN PATIENTS WITH MILD-TO-MODERATE ATROPHIC GASTRITIS: A MULTICENTER RETROSPECTIVE COHORT STUDY BY THE OSAKA GUT FORUM

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Introduction: The development of metachronous gastric cancer (MGC) remains a major problem for the patients who underwent endoscopic resection (ER) against the early gastric cancer (EGC). Preceding studies have shown controversial conclusions regarding the preventive effect of *Helicobacter pylori* (*H. pylori*) eradication on the occurrence of MGC. A reason for the conflicting results may come from the difference of patient characteristics included in each study, especially with regard to the patients' baseline degree of atrophic gastritis.

Aims & Methods: This multicenter retrospective study, conducted at 12 institutions, aimed to evaluate the long-term effects of *H. pylori* eradication by stratifying patients' baseline degrees of atrophic gastritis. A total of 483 *H. pylori*-positive patients who had undergone curative ER for EGC for the first time between 2003 and 2010 were included, and divided into two groups:

- (1) those having undergone successful *H. pylori* eradication within 1 year after ER (eradicated group, n = 294) and;
- (2) those with failed or not attempted *H. pylori* eradication (non-eradicated group, n = 189).

The cumulative incidences of MGC between the two groups were compared for all patients, for mild-to-moderate atrophic gastritis patients (n = 182), and for severe atrophic gastritis patients (n = 301). The degree of atrophic gastritis at the time of ER was assessed by reviewing the recorded endoscopic images, and classified according to the Kimura-Takemoto classification: it was rated as "mild" for C-1 and C-2, "moderate" for C-3 and O-1, and "severe" for O-2 and O-3. MGC was defined as a new cancer developed more than 1 year after ER.

Results: Median follow-up period was 5.2 years (range, 1.1-14.8). Overall, MGC developed in 52 (17.7%) in the eradicated group and in 35 (18.5%) in the non-eradicated group.

For all patients, the cumulative incidence of MGC was lower in the eradicated group than that in the non-eradicated group (13.9% versus 15.7% at 5 years, $P = 0.11$). In patients with mild-to-moderate atrophic gastritis, MGC developed in 15 of 111 patients (13.5%) in the eradicated group and in 16 of 71 patients (22.5%) in the non-eradicated group, and the cumula-

tive incidence was significantly lower in the eradicated group than that in the non-eradicated group (8.7% versus 18.8% at 5 years, $P = 0.03$). In patients with severe atrophic gastritis, MGC developed in 37 of 183 patients (20.2%) in the eradicated group and in 19 of 118 patients (16.1%) in the non-eradicated group, and the cumulative incidences were not significantly different between the two groups (17.1% versus 14.2% at 5 years, $P = 0.69$).

Conclusion: *H. Pylori* eradication had a preventive effect on the development of the metachronous gastric cancer in patients with mild to moderate atrophic gastritis.

Disclosure: Nothing to disclose

P0181

ENDOSCOPIC MUCOSAL RESECTION VS ENDOSCOPIC SUBMUCOSAL DISSECTION IN THE SHORT-TERM OUTCOMES OF ENDOSCOPIC RESECTION FOR SUPERFICIAL NON-AMPULLARY DUODENAL TUMORS; A MULTI-CENTER RETROSPECTIVE STUDY

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Introduction: The selection of endoscopic treatments for superficial non-ampullary duodenal epithelial tumors (SNADETs) are controversial.

Aims & Methods: We compared the efficacy and safety of endoscopic treatment between endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) for SNADETs.

We conducted a retrospective study by using a database of endoscopic treatment for SNADETs at eight hospitals in Fukuoka, Japan from April 2001 through October 2017. A total of 142 patients with SNADEs treated by EMR or ESD were analyzed. Propensity score matching was applied to adjust for the differences of patients between two groups. We analyzed short-term outcomes including the rates of en-bloc/complete resection, the procedure time, the complication rate and hospital days.

Results: Twenty eight pairs of patients were created. The characteristics of patients among two groups were quite similar after matching. We observed significantly shorter procedure time and hospital days in EMR group than those in ESD group (Median procedure time [interquartile range [IQR]: 8 [6-10.75] vs 11 [8.25-14.75], $p = 0.006$).

Other short-term outcomes were not significantly different between two groups (En-bloc resection rate: 82.1% vs 92.9%, $p = 0.42$, Complete resection rate: 71.4% vs 89.3%, $p = 0.18$, complication rate: 3.6% vs 17.9%, $p = 0.24$). One case in ESD underwent emergent surgery due to intraoperative perforation.

Conclusion: This propensity score matching study suggested that EMR is significantly shorter than ESD in procedure time and hospital days. Curability and safety was not significantly different between both groups. This study suggests that EMR has some advantage in medical cost for the treatment of SNADETs due to shorter procedure time and hospital days.

Disclosure: Nothing to disclose

P0182

SYNCHRONOUS OCCURENCE OF PRENEOPLASTIC LESIONS IN THE UPPER GASTROINTESTINAL TRACT AND CANCER IN PATIENTS WITH LYNCH SYNDROME

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Introduction: Lynch syndrome (LS) is the most common hereditary colorectal cancer (CRC) syndrome and accounts for ~3% of all CRCs. This autosomal dominant disorder is caused by germline mutations in DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, *PMS2* and *EPCAM*). Approximately one in 279 individuals of the general population is considered to be a carrier of a pathogenic variant. LS patients are at high CRC risk of up to ~50% depending on the affected gene, and also at increased risk to develop metachronous CRC. LS also includes a variety of extracolonic malignancies such as gastric carcinoma (life-time risk 13%) or small bowel cancer (life-time risk 8%). So far, prospective endoscopic data on surveillance of the upper gastrointestinal tract is scarce.

Aims & Methods: Patients with a proven pathogenic mutation in a DNA mismatch repair gene were included in a surveillance program at our National Center of Hereditary Tumor Syndromes according to the recommendations of the German Consortium for Familial Intestinal Cancer. Patients were included in the final analysis if they received at least one esophagogastroduodenoscopy (EGD) at our center. Results of endoscopy, histopathology, affected gene and occurrence of other malignancies were compared. Synchronous occurrence of malignancies was defined as cancer being detected six month before or after EGD.

Results: A pathogenic MMR gene variant was detected in all patients (48 *MLH1* (38%); 57 *MSH2* (46%); 18 *MSH6* (14%); 2 *PMS2* (2%)). In 6 patients, a prior small bowel cancer was diagnosed (2 *MLH1*, 2 *MSH2*, and 2 *MSH6*). At least one EGD with mucosal biopsy was performed in 125 proven mutation carriers (female 47%) since 2008 (2.5 EGD/patient; range 1-11). An endoscopic follow-up was done with a median time of 36 months, in total a follow-up time of 2948 patient/months.

One esophageal leiomyoma was detected in one patient. Barrett esophagus was detected in 11 patients (9%), one with high-grade dysplasia. Gastritis was histopathological proven in 90 patients (72%), with underlying *Helicobacter pylori* infection in 16 cases (13%). In 22 patients (18%) intestinal metaplasia was found, in one patient (*MLH1*) with dysplasia.

Overall, gastric or small bowel cancer was diagnosed in 6% of the patients. Two new cases of gastric cancer, two new cases of duodenal cancer and one ampullary cancer were observed (age 50-65 years) during routine endoscopic surveillance. Two symptomatic patients were diagnosed with small bowel cancer (jejunum and ileum). Three gastric adenomas and five duodenal adenomas were detected (age 32-65 years). The detection of (pre-) neoplastic upper gastrointestinal lesions was often associated with the occurrence of synchronous LS-associated cancer (5/10 patients, 50%).

No difference was noted between *MLH1* (5 cases) or *MSH2* mutations (5 cases). No lesions were observed in *MSH6* or *PMS2* mutation carriers. Adding prior small bowel cancer, in 10/125 (8%) patients small bowel cancer was observed.

Conclusion: This prospective endoscopic study shows that surveillance of the upper GI tract identifies clinically relevant results in a large proportion of LS patients. Interestingly, the synchronous occurrence of upper GI neoplastic lesions and LS-associated cancers shows the systemic effect of the disease. Further studies are needed to determine surveillance intervals and gene specific tailored approaches.

Disclosure: Nothing to disclose

P0183

BIOLOGIC BEHAVIORS OF THE EARLY GASTRIC SIGNET RING CELL CANCER AND HISTOLOGY BASED PREDICTION OF LYMPH NODE METASTASES

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Introduction: The behavior of signet ring cell carcinoma (SRCC) in early gastric cancer (EGC) is still controversial. This study aimed to compare clinicopathologic features in different histologic type of Chinese EGC patients and to establish a prognostic nomogram for identifying lymph node metastasis (LNM) in EGCs.

Aims & Methods: We reviewed records of EGCs who undergone surgical resection between 2013 and 2017 in a tertiary hospital in Jiangsu province, China. We divided EGC into pure SRCC, mixed SRCC, and NSRC and reviewed the clinical data, endoscopic features, and pathological data. Then, we built a nomogram based on independent risk factors for LNM prediction.

Results: A total of 1008 EGCs were enrolled. 16.2% patients were classified as SRCC, including 63 cases of pure SRCC and 100 mixed SRCC. The SRCC group was more associated with younger age, male, middle and lower location, mucosa-confined and LNM than NSRC group. Further stratification analyses demonstrated that mixed SRCC were associated with an increased risk of LVI ($P = 0.032$) and LNM ($P < 0.001$), in contrast with pure SRCC. By multivariate logistic regression, female, tumor size ≥ 2 cm, flat type, submucosa invasion, LVI, located in middle part and mixed SRCC were independent predictors of LNM in SRCC. No nodal metastases were observed in pure signet ring cell carcinomas ≤ 1 cm without lymphovascular invasion and confined to the mucosa.

Conclusion: Mixed SRCC in EGCs showed more aggressive behavior. Therefore, more attention should be paid to the purity of the SRCC component in clinical practice.

Disclosure: Nothing to disclose

P0184

THE POSITION OF DUODENAL STENT INSERTION ENHANCES STENT PATENCY IN PATIENTS WITH UNRESECTABLE PANCREATOBILIARY CANCERS

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Introduction: Gastric outlet obstructions are common complications associated with pancreatobiliary cancers¹. Gastroenteric bypass surgery is initially used to treat gastric outlet obstructions, but is associated with significant risks of morbidity, mortality and delayed gastric emptying². Therefore, duodenal stent placement is becoming an alternative way to treat gastric outlet obstructions, the position of which is recommended that it does not impose on the papilla of Vater, because it is desirable to keep the route of the biliary stent insertion open³. However, there are few reports available that emphasize the impact of stent positioning.

Aims & Methods: The purpose of this study is to assess the effectiveness of stent positioning by evaluating stent patency with a particular focus on the positional relationship between the oral-site end of the duodenal stent and the pylorus. We defined stent obstructions as follows: (a) when the stent dysfunctions were proven by endoscopy, and (b) when the patient would vomit. This retrospective and single-center study included patients with unresectable pancreatobiliary cancers treated with duodenal stents between March 2013 and March 2020, and they were assessed until April 2020. The study protocol was approved by Sendai Kousei Hospital, and we obtained patient acceptability of opt-out consent for this study. The patients were divided into two groups based on where the stent was inserted: the proximal group, in which the oral-site end of the duodenal stent was placed in an area proximal to the pylorus; and the distal group, in which the stent was placed in an area distal to the pylorus. The rate of stent patency was assessed by Kaplan-Meier analysis, and at 30, 60, 90, and 120 days after the stent insertion by chi-square test. A P -value $< .05$ was considered to indicate statistical significance.

Results: 36 patients were enrolled in this study, with 12 patients in the proximal group and 24 patients in the distal group. The patient demographics and clinical characteristics are summarized in Table 1. The period of stent patency is significantly longer in distal group than in proximal group in Kaplan-Meier analysis ($P=0.019$), especially at 30 days after insertion by chi-square test (30 days: $P=0.018$, 60 days: $P=0.068$, 90 days: $P=0.10$, 120 days: $P=0.14$).

Conclusion: Duodenal stent patency could be enhanced in patients with unresectable pancreatobiliary cancers by placing the stent in a position distal to the pylorus. We presume that the appropriate position of the duodenal stent is beneficial for the patients of unresectable pancreatobiliary cancers.

	Proximal group	Distal group
Patients, n	12	24
Age, median (range), years	74 (49-89)	75 (56-90)
Sex, male, n (%)	9 (75.0)	11 (45.8)
Underlying disease		
Biliary tract cancer, n (%)	4 (33.3)	3 (12.5)
Pancreatic cancer, n (%)	8 (66.7)	20 (83.3)
Gallbladder cancer, n (%)	0 (0)	1 (4.2)
Obstruction, n (%)	8 (66.7)	7 (29.2)

[Table 1: Patient demographics and characteristics]

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Disclosure: Nothing to disclose

P0185

ANALYSIS OF VOLATILE ORGANIC COMPOUNDS EMITTED BY GASTRIC JUICE

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Introduction: Currently, volatile constituents of human volatolome are considered to be a reliable and rapid source of information on normal and abnormal physiological processes occurring in the body and have thereby, a great potential for medical diagnosis and therapy. Breath analysis holds in this context a distinguished status as it is non-invasive, real-time and some breath constituents have already been linked to various disease processes including cancer.

However, the main unresolved issue is the poor understanding of the sources and metabolic fate of volatile organic compounds (VOCs) in the human organism. This problem can be addressed via comparing volatile patterns obtained from different sources (fluids, or tissues).

Aims & Methods: The primary goal of this pilot study was to identify volatiles being emitted by gastric juice (GJ) as an alternative source of information on potential gastric cancer markers. A cohort of 10 healthy volunteers were enrolled. For VOCs analysis GJ were collected during gastroscopy.

After collection, all samples were frozen. Gas chromatography with mass spectrometric detection coupled with head-space needle trap extraction as the pre-concentration technique was used to identify and quantify VOCs emitted by GJ.

Results: A total number of 62 compounds have been identified in the headspace of the GJ samples. However, only 33 species exhibited occurrence above 20%. Amongst, them there were several hospital environment related species (propofol, 1-propanol and 2-propanol). The predominant chemical classes were aldehydes and alcohols with fourteen and nine species, respectively. Apart from these, there were six ketones, seven esters, six organic acids, six hydrocarbons, three aromatics and three heterocyclics. Only one compound (acetone) was found in all samples and further three (2-methyl-propanal, 2-butanone and cyclohexanone) in all samples but one. The number of VOCs found in the GJ samples ranged from 14 to 26 (median 23).

Conclusion: Analysis of VOCs emitted by GJ samples provides an opportunity to identify compounds associated with a gastric cancer state. These components in turn could be targeted in breath of gastric cancer patients and thereby assist the non-invasive diagnosis of gastric cancer based on simply in use, portable breath analyzers.

Further studies involving GJ samples obtained from gastric cancer patients and healthy controls are required to detect volatile biomarkers of this disease and to understand their origin and fate in human organism.

Disclosure: Nothing to disclose

P0186

ADDITION OF LINKED COLOR IMAGING TO WHITE LIGHT ENDOSCOPY IMPROVES DELINEATION PERFORMANCE OF EARLY GASTRIC CANCER LESIONS BY NON-EXPERT ENDOSCOPISTS

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Introduction: Early gastric cancer lesions are subtle, focally distributed, and poorly visible endoscopically. Therefore, endoscopists have difficulties evaluating these subtle early gastric cancer lesions.

Aims & Methods: The aim of this study was to evaluate the role of linked color imaging (LCI) for the visualization of early gastric cancer in comparison to white light endoscopy (WLE) alone, when assessed by non-expert endoscopists. 40 unique cases of early gastric cancer, visualized in both WLE and LCI, were collected for this study. To establish ground truth, all cases were delineated by three expert endoscopists from Japan. Using a web based module, these cases were delineated by 48 non-expert endoscopist assessors of four different countries (Japan, Netherlands, Portugal and Sweden). Endoscopic expertise was divided into different levels: fellow in training, junior endoscopist and senior endoscopist. The module consists of three assessment phases, with a wash-out period of 2 weeks in between each phase. Assessment 1: WLE alone; Assessment 2: LCI alone; Assessment 3: WLE+LCI in a side-to-side display. The outcomes of this study were: 1) overlap between assessors' delineation and expert ground truth; 2) assessors' delineation performance in terms of differentiating between neoplastic tissue and normal tissue; 3) ability to delineate the lesions (VAS-scores 1-10); 4) assessors' preferred imaging modality (WLE, LCI or no preference).

Results: Linear mixed-effect models showed a significant increase in assessors' delineation performance from 77% (SD 26%) in WLE alone and 75% (SD 28%) in LCI alone to 81% (SD 24%) when combining both imaging modalities ($P < 0.001$). When differentiating neoplastic from non-dysplastic tissue, the combination WLE+LCI also caused increased performance scores (49% in WLE and 49% in LCI to 53% in WLE+LCI; $P < 0.001$). Japanese assessors performed significantly better than Dutch, Portuguese and Swedish assessors when delineating early gastric cancer lesions, regardless of imaging modality (87% vs. 71%, 72% and 73% respectively; $P < 0.001$). There was no distinction between the different levels of endoscopic expertise. Median VAS scores were higher for phase 2 (6; IQR 5-8) and 3 (7; IQR 5-8) compared with phase 1 (5; IQR 3-7) for the ability to delineate the lesion ($P < 0.001$). Assessors preferred LCI over WLE (72.4% vs. 5.2%, 22.4% no preference) for the appreciation of early gastric cancer lesions.

Conclusion: The combined use of WLE and LCI resulted in enhanced delineation of early gastric cancer lesions by non-expert endoscopists. Although assessors appreciated the ability of LCI for delineation better than WLE, there was no difference in separate delineation scores for LCI and WLE.

Disclosure: Nothing to disclose

P0187

GENETIC COUNSELING FOR GASTRIC AND PANCREATIC CANCER BASED ON SUSPICION CRITERIA IS AN EFFECTIVE STRATEGY FOR DETECTING HIGH-RISK GROUPS

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Introduction: Gastric adenocarcinoma (GC) and pancreatic adenocarcinoma (PC) are in an increasing incidence and entail high mortality, mainly due to their late diagnosis. The identification of high risk groups of GC/PC (hereditary or familial cancers) could imply a benefit in the affected families, by allowing their inclusion in prevention programs adapted to their risk (genetic counseling).

Aims & Methods: To assess the diagnostic yield of hereditary and familial syndromes GC/PC in individuals evaluated in a high-risk cancer clinic based on 3 suspicion criteria: 1) personal history (PH) of GC/PC < 60 years, 2) PH of GC/PC (at any age) and other malignancy and 3) family history (FH): ≥ 2 relatives with GC or PC. Immunohistochemical analysis of DNA mismatch repair proteins (IHC-MMR) was performed in available tumors. A germline genetic analysis was performed if clinical criteria of hereditary syndrome were fulfilled, according to current guidelines^{1,2}. Familial GC (FGC) was defined as ≥3 first or second degree relatives (FDR or SDR) with GC or ≥2 FDR/SDR with GC (at least one < 50 years). Familial PC(FPC) was defined as ≥2 FDR with PC or ≥3 relatives with PC, regardless of the degree and age of the relative. Hereditary GC/PC was defined if known causative mutation was detected. The remaining cases were classified as sporadic. Multivariate logistic regression analysis was performed for identifying variables associated with hereditary basis of GC/PC. We included OR with 95% CIs to quantify the magnitude of the association.

Results: From May 2014 to October 2019, 77 families (45 from GC group and 32 from PC group) were recruited due to pre-selected suspicion criteria fulfillment: 51(66.2%) due to cancer diagnosis < 60 years, 3 (4%) due to GC/PC and PH of other cancer and 23 (29.8%) due to FH. Median age at cancer diagnosis was 49 (interquartile range: 41.5-58) and 46 (59.7%) were female. Nine (11.7%) had PH of other malignancy. IHC-MMR was performed in 38 (49.3%) tumors being pathological in 1(2%) GC. Causative gene mutations were found in 10/22(45.5%) families analyzed [7/16(43.7%) from GC group and 3/6(50%) from PC group (table 1)] and 19 (24.7%) families fulfilled criteria of familial cancer. The remaining 48 (62.5%) cases were classified as sporadic cancers. Diagnosis of cancer ≤40 years and PH of other cancers were independent risk factors of hereditary origin [OR:11.3 (95%IC 1.9-67); p=0.007 and OR: 17.4 (95% IC 2.5-119.9); p=0.004; respectively].

Conclusion: Almost 40% of the families with GC or PC evaluated based on suspicious criteria belonged to a high-risk group of cancer. Alteration of the DNA MMR system is infrequent in this setting; however, the selection of patients based on specific clinical criteria leads to high diagnostic yield, detecting a causative germline mutation in the 45.5% of cases. Given the wide variability of cancer syndromes observed, both meticulous genetic counseling and use of multi-gen panels seems crucial in this ambit. Factors such as young age at diagnosis and previous history of other malignancies may be able to identify patients with hereditary syndromes.

Patient	Group	Age*	Gender	Referral criteria	Other cancer (age)	IHC-MMR	Genetics technique	Mutation	Hereditary Syndrome
1	GC	75	Female	GC+other tumor	Endometrium (53)	MSH2/MSH6 -	Single-gene test	MSH 2	Lynch syndrome
2 and 3	GC	55* and 35*	Both Female	Both Family history	2 - Breast (58) and 3 - Endometrium (58)	Undone	Multigen panel	ATM	ATM-associated hereditary cancer
4 and 5	GC	41 and 38	Both Male	Both GC<60 years	No	Undone	Multigen panel	CDH1	Hereditary diffuse GC syndrome
6	GC	49	Female	GC<60 years	Breast (44)	MMR+	Single-gene test	BRCA 2	Breast and ovarian cancer syndrome
7	GC	34	Male	GC<60 years	No	MMR+	Multigen panel	P53	Li-Fraumeni syndrome
8	PC	45*	Female	Family history	No	Undone	Single-gene test	BRCA 2	Breast and ovarian cancer syndrome
9	PC	33	Male	PC<60 years	No	Undone	Multigen panel	ATM	ATM-associated hereditary cancer
10	PC	33	Male	PC<60 years	No	Undone	Multigen panel	PALB 2	Breast and ovarian cancer syndrome

* If no personal history of GC or PC, the age corresponds to the youngest relative. IHC-MMR: immunohistochemical analysis of DNA mismatch repair proteins; GC gastric cancer, PC: pancreatic cancer.

[Characteristics of the hereditary syndromes detected in the total cohort (77 families)]

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Disclosure: Nothing to disclose

P0188

THE SURVEILLANCE STRATEGY AFTER ENDOSCOPIC OR SURGICAL TREATMENT OF EARLY GASTRIC CANCER

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Introduction: With the increasing detection of early gastric cancer(EGC), minimally invasive treatment methods have been investigated to improve quality of life in patients with EGC, while maintaining survival rates comparable to those with conventional radical gastrectomy. Endoscopic resection, a representative minimally invasive treatment for EGC, is currently recognized as the standard treatment method for this disease in selected case. As the number of patients diagnosed with EGC has been increasing as a result of improved surveillance, it is becoming more important to detect recurrence. However, the surveillance strategy for EGC after the treatment has not yet been well established.

Aims & Methods: To investigate the role of regular endoscopy and computed tomography (CT) scan surveillance after treatment of EGC. Consecutive clinical data of 1,615 patients with 1,692 lesions who had undergone endoscopic or surgical treatment for EGC between 2007 and 2012 were

retrospectively reviewed. All the gastric lesions were completely resected and all of them had one or more endoscopy and CT scan examination during the follow-up.

Results: In endoscopic resection group (434 lesions in 415 patients), 14 revealed metachronous gastric adenocarcinoma, all of which could be detected by endoscopy with biopsy. In surgical resection group (1258 lesions in 1200 patients), 15 patients revealed tumor recurrence, including 6 cases with metachronous gastric adenocarcinoma, 5 with loco-regional recurrence, 1 with regional lymph node metastasis without distant metastasis, and 3 with both lymph node and distant metastases. All metachronous gastric adenocarcinoma and loco-regional recurrent tumors could be detected by endoscopy with biopsy. All the metastasis cases (n = 4) were diagnosed by abdominal CT, and their initial EGC pathologies were all sub-mucosal invasive early gastric cancers with lymph node involvement.

Conclusion: Regular follow-up of both endoscopy and CT scan is necessary after the surgical treatment of EGC; CT scan seems to be more valuable in case of submucosal invasive early gastric cancers and/or lymph node involvement. CT scan might have a limited role for the surveillance after endoscopic resection of EGCs which meet the expended criteria as well as absolute criteria. In view of cost-effectiveness, tailored surveillance strategy might be necessary after treatment of EGCs.

Disclosure: Nothing to disclose

P0189

ASSOCIATION BETWEEN LONG-TERM USE OF PROTON PUMP INHIBITORS AND THE RISK OF GASTRIC CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Current evidence suggests that long-term proton pump inhibitor (PPI) use may be associated with an increased risk of gastric cancer (GC).

Aims & Methods: We conducted a systematic literature review and meta-analysis on the association between PPI long-term use and GC risk. Three independent reviewers systematically searched Ovid MEDLINE and EMBASE (inception-November 2019) according to a predefined protocol in PROSPERO (CRD42018102536) and assessed study quality using the Newcastle Ottawa Quality Assessment Scale.

Reviewers independently extracted data, meta-analyzed available and newly calculated Odds ratios (OR) using a random effects model and stratified for GC site (cardia vs non-cardia) and PPI duration (< 1 year, 1-3 years, >3 years).

Results: We screened 1,734 records and included four retrospective cohort and seven case-control studies of good quality comprising 1,191,285 individuals in our meta-analysis.

We found an increased GC risk in long-term PPI users (OR 2.05, 95% confidence interval [95%CI] 1.49-2.82) in random effect models. Stratified analyses indicated a significant risk increase in non-cardia (OR 2.19, 95%CI 1.27-3.76), but not cardia regions (OR 1.85, 95%CI 0.53-6.45). There was no GC increase with longer durations of PPI exposure (< 1 year: OR 2.29, 95%CI 2.13-2.47; 1-3 years: OR 1.46, 95%CI 0.53-4.01; >3 years: OR 2.08, 95%CI 0.56-7.77).

Conclusion: We found a twofold increased GC risk among long-term PPI users, but this association does not confirm causation and studies are highly heterogeneous.

Long-term PPI therapy should only be prescribed when strictly indicated, and dedicated prospective research is urgently needed.

Disclosure: DS has received traveling fees from AbbVie and a research grant from the Novartis Foundation for medical-biological research unrelated to this work. BM has served at an advisory board for Gilead and Novigenix. He has received speaking fees from Vifor, MSD and Takeda and traveling fees from Vifor, Novartis, MSD and Takeda. He has received a research grant from MSD unrelated to this work. NB and DG have nothing to disclose.

P0190

CLINICAL CHARACTERIZATION AND SCREENING STRATEGIES IN FAMILIAL GASTRIC CANCER: PRELIMINARY RESULTS OF THE FIRST SPANISH MULTICENTER STUDY

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Introduction: Approximately 10% of gastric adenocarcinomas (GC) show familial aggregation, and a hereditary cause is determined in up to 5% (hereditary GC). Familial GC (FGC) is characterized by an autosomal dominant inheritance pattern of GC, without a responsible germline mutation. The clinical characteristics of FGC, the prevalence of GC and GC-Precursor Lesions (GCPL) and the effectiveness of preventive strategies, have been poorly studied.

Aims & Methods: Objective: To describe the clinical and pathological characteristics of FGC, the screening strategies used and estimate the risk of GC and GCPL in this scenario.

Methodology: a multicenter nationwide study with retrospective inclusion of individuals with FGC was performed. FGC was defined as: a) Criterion A: ≥ 2 first-degree relatives (FDR) or second-degree relatives (SDR) affected by GC (≥ 1 diagnosed < 50 years), or b) Criterion B: ≥ 3 FDR or SDR with GC at any age. Clinical data, oncological personal and family history (FH), endoscopic and pathological reports, were collected.

Results: A total of 69 patients (50 families) were included from 11 Spanish centers: the median age was 59 years (range 46-71) and 37 (53.6%) were women. The criterion A of inclusion was fulfilled by 37,7% of the cases and criterion B was present in the remaining 62.3% individuals. Prevalence of smoking history and chronic alcohol consumption was 38% and 9.4%, respectively. In 14 (20%) cases, personal history of extra-gastric malignancies was reported (3 breast, 2 colorectal, 2 prostate, 2 melanoma, 2 leukemia, 3 other cancers).

Twenty-one (30.4%) patients, corresponding to 18 families, developed GC at a median age of 63 years (range 47-73) and 2 (9.5%) of them were diagnosed during screening endoscopy. Diffuse histology was reported in 10

(47.6%) cases and 13 (62%) tumors were detected in advanced stages (III/IV). Gastrectomy was performed in 14 (66.6%) patients: 9 (64%) total and 5 (36%) partial gastrectomy. Eight (38%) patients died due to this neoplasia. Regarding screening, gastroscopy was performed in 47 (68.1%) individuals, with a total of 176 explorations: in 42 (89.3%) cases random biopsies were taken [(Sydney protocol in 7 (14.9%) and Cambridge protocol in 4 (8.5%)], in 31 (66%) *helicobacter pylori* (HP) infection was tested and no biopsies were taken in the remaining 5 (10.7%) cases. Median age at first screening endoscopy was 50.5 (range 36–56) years, with a median of 3 (range 1–5) procedures and a median surveillance of 4 (range 1–12) years. Overall, HP was investigated in 39 (56.5%) individuals, being positive in 24 (61.5%).

During endoscopic screening, 19/47 (40.4%) GCPL were detected (if more than one in the same patient, the most advanced lesion is specified): complete or incomplete intestinal metaplasia in 6 (12.7%) and 5 (10.6%), respectively; extensive atrophic gastritis in 4 (8.5%), low and high-grade dysplasia in 3 (6.3%) and 1 (2.1%), respectively. Moreover, invasive GC was detected by screening gastroscopy in 2 (4.2%) patients, both in an early stage (I and II).

Conclusion: Despite previous family history, the majority of GC within a cohort of individuals of FGC, were diagnosed at advanced stage.

Whereas endoscopic screening was performed in nearly 70% of individuals with FGC, HP infection was investigated in just over half.

Up to 45% individuals of FGC under endoscopic screening were diagnosed with GC-precursor lesions and early stages GC.

Definitive results of our study could improve the characterization of FGC in order to determine the best prevention measures for these patients.

Disclosure: Nothing to disclose

P0191 WITHDRAWN

P0192 WITHDRAWN

P0193

SEROLOGICALLY DETERMINED GASTRIC ATROPHY ASSOCIATED WITH LIFESTYLE, DIETARY FACTORS AND *HELICOBACTER PYLORI* STATUS

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Introduction: Serum pepsinogen (Pg) is regarded the best non-invasive method of assessing gastric mucosal status and has a moderate diagnostic yield in detecting precancerous changes with substantial heterogeneity between studies, possibly due to unaccounted population factors [1]. Although there is strong evidence implicating *H. pylori* (HP) and genetics in the development of gastric atrophy and cancer, data on the role of lifestyle and dietary factors, especially pertaining to atrophic gastritis, remains controversial.

Aims & Methods: A total of 2055 participants aged 40–64 years from the “*Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR) study” in Latvia were tested for Pgl and Pgli by latex-agglutination (Eiken Chemical, Japan). HP presence was detected by ¹³C-urea breath test. Data on gender, age, education, employment, dietary intake including alcohol, exercise, smoking, BMI, and proton pump inhibitor use (PPI) was obtained by survey and compared for

those with and without serologically detected gastric atrophy (sGA) (cut-off values Pg I/Pg II ≤2 and Pg I ≤30 ng/mL as determined previously) [2]. A supplementary analysis with a second group of participants (1578) of the GISTAR study with HP determined by serum IgG antibodies (>30 ng/ml) instead of UBT was performed as described above to assess for differences based on the method used to identify HP infection.

Results: Almost half of the participants included (mean age 52.2 years SD±6.8, 42.5% male) were HP positive (48.7%) and 7.3% had sGA. Multivariate analysis included age, gender, employment, HP, consumption of salted, pickled products, onion, fruit/vegetables and instant coffee, daily meals and PPI use. Smoking and alcohol were additionally included based on the evidence from previous studies.

In multivariate analysis sGA was significantly associated with age (OR 1.1 per year increase; 95% CI 1.0, 1.1), frequent consumption of salted products (1.6; 1.0, 2.6), onion (3.0; 1.4, 6.8), and instant coffee (1.5; 1.0, 2.1), but inversely with current smoking (OR 0.6; CI 0.4, 0.9), HP detected by UBT (0.4; 0.3, 0.6), frequent consumption of pickled products (0.2; 0.1, 0.7) and PPI use in the past month (0.5; 0.2, 0.9). In the second group, sGA was associated with age (OR 1.0 per year increase, 95% CI 1.0, 1.1), male gender (1.8; 1.2, 2.9), frequent consumption of salted products (3.1; 1.3, 7.2), instant coffee (1.6; 1.1, 2.4), and having five or more vs. two to three meals per day (2.3; 1.5, 3.4), but inversely with being employed (0.5; 0.3, 0.8), current smoking (0.6; 0.3, 1.0), and frequent consumption of pickled products (0.3; 0.1, 1.2). In the second group, there was a tendency towards an association between sGA and HP seropositivity, but was not statistically significant (OR 1.5; CI 1.0, 2.3; p = 0.06).

Conclusion: Serologically determined gastric atrophy was positively associated with several dietary factors which have also been linked to the risk of gastric cancer, and inversely with smoking. The nature of the association with *H. pylori* seemed to depend on the method used to detect HP. Further analysis to determine if these factors are linked to the diagnostic yield of Pg, and whether their effects are modified by *H. pylori* presence, could be useful in improving the detection of individuals at increased risk of gastric cancer.

References: 1. Bang CS et al. Prediction of Chronic Atrophic Gastritis and Gastric Neoplasms by Serum Pepsinogen Assay: A Systematic Review and Meta-Analysis. J Clin Med. 2019; 8(5):657. 2. Leja M et al. Detection of gastric atrophy by circulating pepsinogens: A comparison of three assays. Helicobacter 2017;22:e12393.

Disclosure: The study was funded by project nr. lzp-2018/1-0135 “Research on implementation of a set of measures for prevention of gastric cancer mortality by eradication of *H. pylori* and timely recognition of precancerous lesions” of the Latvian Council of Science. The authors declare no conflict of interest.

P0194

EVALUATION OF KI67 INDEX FOR THE ASSESSMENT OF MALIGNANCY RISK IN GASTRIC GASTROINTESTINAL STROMAL TUMORS

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Introduction: The risk of malignancy in gastrointestinal stromal tumors (GISTs) is determined by assessing the resected tumors according to the risk classification systems, that are based on tumor size, location, and mitotic index. Recent studies has focused on assessing other prognostic factors to precisely predict the prognosis. Ki67, a cell cycle marker, index in resected samples has been reported to have a prognostic value in GISTs and furthering the ascertainment of proliferation rate in addition to mitot-

ic index. The feasibility of the classification systems using EUS-guided fine needle aspiration (FNA) samples is not accepted, because mitotic index can not be assessed on FNA samples, even in high-risk tumors. However, Ki67 can be assessed on FNA samples. In this study we aimed to analyse the accuracy of EUS-FNA of later resected GISTs in reference to Ki67 index as taking surgical samples gold standard.

Aims & Methods: We retrospectively analyzed 55 patients who underwent EUS followed by surgical resection for gastric GIST between October 2010 and December 2019 at a single tertiary center. Data investigated in this study included age, sex, tumor size, location, mitotic index, cell type (spindle, epithelioid, or mixed), cellularity (mild, moderate or high), pleomorphism, presence of ulceration, hemorrhage, necrosis, and invasion, growth pattern (expansile or infiltrative), and Ki67 index.

Results: The median age was 56 years (range 22-78), there were 35 female and 20 male patients. Localization of GISTs were cardia 10, fundus 9, gastric body 22, and antrum 14. The median tumor size was 40 (range: 20-200) mm. We coalesced the patients into a low-risk (very low-risk was considered low-risk) and a high-risk groups (intermediate-risk group was considered high-risk) for further analysis according to Armed Forces Institute of Pathology (AFIP) risk classification. In univariate analysis, excluding tumor size and mitotic index that are already features determining classification, fundus location ($P = .019$), ulceration ($P = .022$), hemorrhage ($P = .016$), mucosal invasion ($P = .026$), and Ki67 index ($P = .020$) were higher in high-risk group, but in the multivariate analysis, only presence of bleeding and Ki67 index were only significant factors ($P = .034$ and $P = .018$) in surgical samples. The best cut off level of Ki67 between low-risk and high-risk groups was 5%, with a sensitivity of 88.2%, specificity of 52.8%, PPV of 46.9%, and NPV of 90.5% ($P = .021$). In addition, a level of Ki67 index over 5% was correlated with high mitotic index, with a sensitivity of 87.5%, specificity of 51.4%, PPV of 43.8%, and NPV of 90.5% ($P = .032$). The mean Ki67 index was lower on EUS-FNA samples than on surgical specimens [2% (1-15) vs. 10% (1-70), $P = .001$]. In addition, the intra-class correlation coefficient value of Ki67 that was .199 ($P = .362$) between FNA and surgical samples showed no reliability of FNA samples.

Conclusion: Expression of Ki67 on resected samples was correlated with high-risk GISTs, although it has no additive value and Ki67 index on FNA samples was not correlated with surgical results.

Disclosure: Nothing to disclose

P0195 WITHDRAWN

P0196

ELASTOGRAPHY IN UPPER GASTROINTESTINAL TRACT SUBEPITHELIAL TUMORS

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Introduction: Subepithelial tumors (SETs) are lesions growing under the intact epithelium. Endoscopic ultrasonography (EUS) is a standard in SET diagnostics. The possibility of increasing the accuracy of the EUS is elastography (EG). EG is an ultrasonographic modality that allows to assessed tissue elasticity. In the study, we focused on the possibilities of using EG in EUS examinations in order to differentiate malignant SETs and specify their diagnosis.

Aims & Methods: 22 patients aged 18 to 73 were enrolled in the study. 12 gastric tumors, 5 duodenal tumors and 4 esophageal lesions were evaluated. The EG image was evaluated qualitatively by a 4 and 5 grade classification system for endoscopic EG and semi-quantitatively using strain ratio (SR) and strain histogram (SH).

	Gender (male/female)	Age (in yr.) median	esophagus/stomach/duodenum	Layer (1/2/3/4)	Dimensions (mm) median
Leiomyoma	3/0	62 (61 - 67)	3/0/0	0/2/1/0	14,5 (14,5 - 21,4)
Lipoma	0/1	27	0/1/0	0/0/1/0	10
Inflammatory fibroid polyp	1/0	45	0/1/0	0/1/0/0	4,1
Neuroendocrine tumor	4/3	59 (29 - 74)	0/5/2	0/2/5/0	9,2 (7 - 13,2)
Adenoma	1/2	56 (49 - 64)	0/0/3	3/0/0/0	13 (10,8 - 18,7)
Gastrointestinal stromal tumor	1/1	56,5 (56 - 57)	0/2/1	0/0/0/2	19 (15 - 23,1)
Aberrant pancreas	0/2	45 (30 - 60)	0/2/0	0/0/2/1	12 (10,6 - 13,5)
B-lymphoma	1/0	56	0/1/0	1/1/1/1	12,6
Spino-cellular carcinoma	1/0	65	1/0/0	1/0/0/0	31,2

[Characteristics of patients, localization and size of subepithelial lesions.]

Results: Using a 5-grade classification system, a value of 1, 2 in 80% and a value of 3, 4, 5 in 20% were assigned to benign tumors. Malignant lesions grade 3, 4, 5 was assigned in 87.5% and 1, 2 in 12.5%. In the 4-grade classification system, the values of 1, 2 were observed in 80% and 3, 4 in 20% of the benign lesions. In contrast, malignant tumors were assigned values of 3, 4 in 87.5% and 1, 2 in 12.5%. The median SR for benign tumors was 6.51 (0.64-15) and the median SH 71 (16-185). In the group of malignant tumors, the median SR was 6.195 (1.5-33), SH 40.19 (14-98).

Conclusion: A high sensitivity and specificity of the 5 and 4-grade classification to distinguish pancreatic malignant lesions is reported in the published literature. SR values above 6.04 and SH below 175 are typical of pancreatic malignant lesions. Significantly different SR and SH values from other lesions in the group were seen in inflammatory polyp and neuroendocrine tumors. According to our observations, the use of a 5-grade scale for evaluating the EG image in combinations with semi-quantitative methods of SR and SH appears to distinguish malignant SETs as the most promising. Further studies with a larger number of patients will show the utility of elastography in differential SET diagnosis.

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Disclosure: Nothing to disclose

P0197

FACTORS ASSOCIATED WITH GASTRIC ATROPHY “MISSED” BY SEROLOGIC TESTING

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Introduction: Serum pepsinogen (Pg) is regarded as the best non-invasive method of assessing gastric mucosal status and has a moderate diagnostic yield in the detection of precancerous lesions and gastric cancer with substantial heterogeneity between studies, possibly due to unaccounted population factors [1].

Identifying factors that may substantially impact Pg values and adjusting Pg cut off values accordingly could potentially improve the diagnostic yield of Pg in detecting gastric atrophy.

Aims & Methods: Participants aged 40-64 years from “*Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR) study” in Latvia with moderate to severe gastric atrophy confirmed by biopsy were tested for blood Pgl, PglI by latex-agglutination (Eiken Chemical) and *H. pylori* (HP) IgG antibodies (Biohit). They were then divided into two groups based on whether gastric atrophy was also identified serologically (where Pg I/Pg II ≤ 2 and Pg I ≤ 30 ng/mL) [2]. Those with gastric atrophy on biopsy and by serology were placed in the serologically determined gastric atrophy group (sGA), while those not identified by serologic testing were placed in the “missed” gastric atrophy group (mGA). Factors associated with decreased Pg were compared between sGA and mGA- gender, age, employment, consumption of ≥ 400 g fruit/vegetables daily, frequency of having salted, pickled products, coffee and allium vegetables, daily meals, smoking, proton pump inhibitor use (PPI), as well as having alcohol and fish, exercise, BMI and self-reported history of peptic ulcer disease based on previous studies.

Results: Out of 1196 participants, 138 (11.5%) had moderate to severe gastric atrophy. A total of 108 cases which had data on *H. pylori* were included in the analysis - 59.3% were male and 79.6% were HP positive. Of these, gastric atrophy was “missed” by Pg testing in 37 (34.3%). The median age for mGA was slightly lower than sGA (54.0, IQR 11 vs. 57.0, IQR 10 respectively, $p = 0.03$). Based on univariate analysis, factors with $p < 0.10$ (age, *H. pylori*, peptic ulcer disease and daily meals) were included in multivariate analysis with gender, employment, smoking and PPI use included additionally based on previous studies. In multivariate analysis, mGA was significantly associated with male gender (OR 4.27, 95% CI 1.11, 16.40), current smoking (OR 5.9; CI 1.4, 24.4), and inversely with HP (OR 0.3; CI 0.1, 0.8) and having five or more versus three to four meals per day (OR 0.07; CI 0.01, 0.7) when compared to sGA. This means that gastric atrophy was more likely to be “missed” by serologic Pg testing in men, current smokers, those seronegative for HP, and those having 3-4 meals per day.

Conclusion: The likelihood of gastric atrophy being missed by serologic pepsinogen testing was increased by several factors, suggesting that adjusted Pg cut-off values for specific subsets of the population (by gender, HP seropositivity, smoking status) might improve the diagnostic yield of Pg testing. A more detailed analysis in a larger population sample is necessary to determine the significance of the application thereof.

References: 1. Bang CS et al. Prediction of Chronic Atrophic Gastritis and Gastric Neoplasms by Serum Pepsinogen Assay: A Systematic Review and Meta-Analysis. J Clin Med. 2019; 8(5):657. 2. Leja M et al. Detection of gastric atrophy by circulating pepsinogens: A comparison of three assays. Helicobacter 2017;22:e12393.

Disclosure: The study was funded by project nr. lzp-2018/1-0135 “Research on implementation of a set of measures for prevention of gastric cancer mortality by eradication of *H. pylori* and timely recognition of precancerous lesions” of the Latvian Council of Science. The authors declare no conflict of interest.

P0198

PROGNOSTIC AND SURVIVAL FACTORS OF GASTRODUODENAL NEUROENDOCRINE TUMORS: OUR CENTER’S EXPERIENCE

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Introduction: Gastroduodenal neuroendocrine tumors represent a rare group of neoplasms, with an incidence of approximately 0.5 in 100000 inhabitants, constituting a small percentage of the gastroduodenal neoplasms. This study evaluated the location, type of primary tumor, degree of systemic attainment as well as other relevant clinical-pathological aspects with an impact on overall survival and disease-free survival

Aims & Methods: We retrospectively evaluated 38 patients with gastric and duodenal neuroendocrine tumors with anatomopathological diagnosis confirmed by biopsies as well as resected specimens in a tertiary referral center between 2008 and 2020.

Patients with MEN-1 (Type 1 Multiple Endocrine Neoplasia) or Von Hippel-Lindau Syndrome were excluded.

Results: There were 20 resected specimens and 18 biopsies. The most frequent primary location was the duodenum with 31 patients (82%), with just 7 patients with primary location in the stomach (18%). The most patients were female (21 patients; 55%). Mean age at diagnosis was 51.2 years (range 19-87 years). The median survival was 156 months. Regarding the existence of metastasis in the time of diagnosis (synchronous or metachronous), were present in 13 patients (34%). Regarding the therapeutic approach, patients underwent surgery (68% - 26 patients), surgery + chemotherapy (24% - 9 patients) or chemotherapy alone (8% - 3 patients). Survival was higher in patients undergoing surgery ($P < 0.001$).

Spearman correlation was used to correlate Ki67, tumor grade and mitotic count. There was a strong correlation between Ki67 and mitotic count and also between Ki67 and tumor grade. We found only a moderate correlation between mitotic rate and tumor grade.

It should be noted that the patient’s age over 65 years at diagnosis ($P < 0.001$), the size of the primary tumor greater than 25 mm ($P = 0.04$), the presence of synchronous metastasis ($P = 0.04$) and the presence of a Ki67 $> 5\%$ ($P = 0.02$) proved to be independent factors of adverse prognosis.

Conclusion: The clinical presentation and biological behavior of gastroduodenal neoplasms varies considerably. In line with previously published case series, the patient’s age less than 65 years, the size of the primary tumor and the absence of locoregional disease, angioinvasion and metastasis are associated with a better prognosis.

Disclosure: Nothing to disclose

P0199

PREDICTORS TO RESISTANT TO QUIT SMOKING AFTER DIAGNOSIS OF GASTROINTESTINAL CANCER AMONG GASTROINTESTINAL CANCER SURVIVORS: NATION WIDE STUDY

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Introduction: Cessation of smoking is essential to improve cancer related outcomes among gastrointestinal cancers (GIC) survivors. However, few studies have assessed the determinant factors to resistant to quit smoking after diagnosis of GIC.

Aims & Methods: We aimed to investigate the predictors to resistant to quit smoking after diagnosis of GIC.

Total of 625 GIC survivors (age≥40 years, median 7.1 years of follow up) from the HEXA Study (2004-2016) were included in this study. Smoking status at diagnosis of GIC cancer was investigated. After exclusion of never smoker, GIC survivors were classified in to quitters and non-quitters according to the smoking status at the diagnosis of GIC. To evaluate the determinant factors to quit smoking after diagnosis of GIC, we used a univariate and multivariate regression analyses between two groups (quitter vs non quitter).

Results: The overall smoking cessation rate was 60.3% (n=226 of 375) among current smoker at the time of diagnosis of GIC. In univariate analysis, female gender (7.7% vs 1.7%, p=0.006), current high risk drinking (72.9% vs 41.4%, p< 0.001), obesity (23.3 ±3.0 vs 22.6 ±2.6, p=0.02) were more prevalent in non-quitter group than quitter group with statistical significance. In multivariate analysis, low household income(Odds ratio(OR) 1.2, 95% confidence interval(CI): 1.1-2.0), current high risk drinking(OR1.4, 95%CI: 1.1-1.9), no regular exercise(OR 1.6, 95%CI:1.3-2.9) smoking duration more than 30 years(OR 1.3, 95%CI:1.1-1.9), and heavy smoker (≥25 cigarettes /day) (OR 1.5, 95%CI:1.1-2.5) were the independent risk factors to resistant to quit smoking after diagnosis of cancer even after adjusting after adjusting cancer type, treatment status, age at diagnosis of GIC, the smoking age, education status, income status, work type, cancer related factors.

Conclusion: Given that smoking cessation is important for GIC survivors' prognosis, it is necessary for physicians to pay attention to survivors who have determinant factors to resistant to quit smoking with monitoring and educating carefully.

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Disclosure: Nothing to disclose

P0200

COMPREHENSIVE EVALUATION OF FIVE RECQ DNA-HELICASE FAMILY MEMBERS EXPRESSION AND ITS PROGNOSIS VALUE IN HUMAN GASTRIC CANCER

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Introduction: The RecQ DNA helicase families including five members -RECQL, Bloom (BLM), Werner (WRN), RECQL4, and RECQL5, play an important role in maintaining genome integrity. Although several studies have reported that RecQ DNA helicase families was closely correlated with the susceptibility to liver cancer and breast cancer, the effect on prognosis in gastric cancer was not yet clarified. Here, we analyzed the expression, prognostic values and clinical characteristics of RecQ family members in gastric cancer.

Aims & Methods: mRNA-expression levels of RecQ members were analyzed via the Tumor Immune Estimation Resource (TIMER) and Oncomine database site. We evaluated the influence of RecQ members on clinical characteristics and prognosis using Gene Expression Profiling Interactive Analysis (GEPIA), MEXPRESS(<https://mexpress.be/index.html>), and Kaplan-Meier plotter. The functionsof the five RecQ family members at the gene and protein levels were explored by the tool of GeneMANIA. The Database for Annotation, Visualization, and Integrated Discovery (DAVID) services provided the Gene ontology enrichment analysis and KEGG pathway analysis.

Results: All members of the RecQ family were highly expressed in most tumors tissues compared to normal tissues. The expression levels of the RecQ family members were correlated with tumor stage, family history of stomach cancer, barrette's esophagus, sample type, histological type, gender, and sample type. High mRNA expression of RECQL was significantly related with poor overall survival (OS), first progression (FP), and post progression survival (PPS) in all gastric cancers. In contrast, high mRNA expression of BLM, RECQL4, and RECQL5 was associated with better OS, FP, and PPS in gastric patients. In addition, Survival analysis revealed that high transcription levels of RecQ members were associated with OS, FP, and PPS in patients with HER2 status, different treatment, stage, differentiation, and lauren classification gastric cancer.

Conclusion: Taken together, these data indicate that RECQL may become a new potential therapeutic target for patients with gastric cancer and that BLM, RECQL4, and RECQL5 may be useful as prognostic biomarkers for gastric cancer. Further research is required to better understand the role of the RecQ genes.

Disclosure: Nothing to disclose

P0201

IDENTIFICATION OF NEW GENES INVOLVED IN GERMLINE PREDISPOSITION TO EARLY-ONSET GASTRIC CANCER

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Introduction: Gastric cancer is the fifth most common cancer worldwide, showing a high mortality rate. Although the majority of gastric cancers cases are sporadic, 10% of them show familial aggregation and a genetic cause is present in up to 5% of all cases. The main associated inherited syndrome is hereditary diffuse gastric cancer, which is mainly caused by *CDH1* mutations. However, the genetic cause for a high number of families with gastric cancer aggregation is unclear, especially in early-onset patients.

Aims & Methods: The aim of the present study was to identify new candidate genes involved in germline predisposition to gastric cancer. For this reason, whole-exome sequencing (WES) of germline samples was performed in 20 patients with gastric cancer before the age of 50 and without *CDH1* mutations at germline level. Nine tumor samples were also available, and WES was also performed. Sequencing data of germline samples were filtered by a pipeline to select those variants with plausible pathogenicity, rare frequency in the general population and previously involved in cancer. After that, a manual filtering was performed in order to prioritize genes previously involved in germline predisposition to any type of cancer and other genes according to current knowledge and gene function. These genetic variants were prevalidated with Integrative Genomics Viewer (IGV). In addition, data of tumor samples was used to analyze its tumor profile using SigProfilerWeb. Subsequently, a selection step was performed according to gene function and information obtained from analysis of tumor samples. Selected variants were validated by Sanger sequencing.

Results: After manual filtering, 274 genetic variants located on 205 different genes were prioritized. Using IGV, 86 genetic variants in 41 genes were discarded. Among the remaining genetic variants, 60 of them corresponding to 54 genes were selected and Sanger sequencing was performed. Finally, 58 final genetic variants in 52 different candidate genes were validated (Table 1).

Function	Genes
Germline cancer predisposition	<i>APC, ATM, SDHC, COL7A1, GPC3, RNF43, EXT2, POLD1, EXT1, POT1, PTCH1, POLH, GATA2, BAP1, ERCC2</i> and <i>FANCA</i>
Cell adhesion	<i>FAT1, FAT2, FAT4</i> and <i>CTNND1</i>
Tumor suppression genes	<i>PHF2, LARP7, LRP1B, WWOX, ADAMTS9, LATS1, BCL6B, ITIH5, NEO1, MAD1L1, GPX7, IQGAP2, DACT2, SIRT3, RCC1</i> and <i>EPHB2</i>
<i>Helicobacter pylori</i> recognition	<i>IL12A, TLR1, TLR2, TLR5, TLR10, A4GNT</i> and <i>MUC1</i>
DNA repair	<i>UNG, KAT5, RAD23A, HBP1</i> and <i>LIG3</i>
Other related functions	<i>ARID4A, ARID1B, ATP4A</i> and <i>ROBO1</i>

[Table 1. Final candidate genes to gastric cancer predisposition.]

Conclusion: Among 52 candidate genes, *APC, FAT4, CTNND1* and *TLR2* seem to be the most promising ones because of their involvement in germline predisposition to hereditary cancer syndromes or in important functions such as tumor suppression, cell adhesion and *Helicobacter pylori* recognition, respectively. Although replication in a different cohort and functional studies will be needed, this project will be helpful to increase the knowledge of predisposition to early-onset gastric cancer.

Disclosure: Nothing to disclose

P0202

LONG NON-CODING RNA POLYMORPHISMS AND RISK OF GASTRIC CANCER AND ATROPHIC GASTRITIS

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Introduction: Long noncoding RNAs (lncRNAs) are greater than 200 nucleotides in length and do not encode functional proteins. They regulate gene expression through various processes, such as chromatin modification, transcription and post-transcription processing. Accumulating evidence shows that lncRNA single nucleotide polymorphisms (SNPs) play an important role in the carcinogenesis of various tumours.

Aims & Methods: The aim of this study was to assess the associations of lncRNA rs217727, rs3200401, rs17840857, rs1054000, rs17694493, rs1333045, rs1011970 polymorphisms with gastric cancer (GC) and atrophic gastritis (AG). SNPs were analyzed in 613 GC patients, 118 patients with AG and 476 controls from 3 tertiary centres in Germany, Lithuania and Latvia. All patients were of European descent. Genomic DNA was extracted from peripheral blood leukocytes using the salting-out method. SNPs were genotyped by the real-time polymerase chain reaction. Associations between gene polymorphism, GC and AG were evaluated using multiple logistic regression analysis with adjustment for sex, age and country.

Results: The prevalence of several genotypes differs between AG patients and controls. CT genotype of rs3200401 was more prevalent in AG patients than in controls (39.3% and 25.5% respectively, $p=0.014$). The same association was found for TG genotype of rs17840857 (48.3% in AG patients and 38.7% in controls, $p=0.029$). The frequency of T allele was 36.0% in AG patients and 27.4% in controls ($p<0.009$). CG genotype of rs17694493 was less prevalent in AG patients than in controls (16.9% and 26.9% respectively, $p=0.005$). Lower prevalence of CT genotype of rs1333045 was also observed in AG patients compared to controls (39.7% and 51.7% respectively, $p=0.019$). No statistically significant differences in the distribution of genotypes and alleles were found between GC patients and controls. Logistic regression analysis revealed that only one polymorphism (rs17694493) was associated with an increased risk of GC. Carriers of GG genotype had higher odds of GC when compared to CC genotype (OR - 4.93; 95% PI 1.28 - 19.00, $P=0.02$). More associations were found between analyzed genotypes and AG. Carriers of CT genotype of rs3200401 had higher odds of AG than those with CC genotypes (OR - 1.81; 95% PI 1.17-2.80, $p=0.007$). OR for AG was 1.61 (95% PI 1.04-2.50, $p=0.034$), when TG genotype was compared with TT genotype of rs17840857. GG genotype of rs17694493 as associated with higher odds of AG than CC genotype (OR 5.11; 95% PI 1.10-23.80, $p=0.038$). Higher odds were found for a recessive

sive model for rs1333045, where comparison of CC vs TT+CT genotypes showed an increased risk of AG (OR 1.88; 95% PI 1.19-2.95, $p=0.007$).

Conclusion: rs17694493 SNP is associated with increased risk of GC and AG, while polymorphisms of rs3200401, rs17840857, and rs1333045 are linked with risk of AG.

Disclosure: Nothing to disclose

P0203

INTRODUCING MENTAL HEALTH INTO GI CLINICS - INTEGRATING THE BRAIN AND THE GUT

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Introduction: Anxiety and Depression are highly prevalent in the Gastroenterology patients. Even with this knowledge, patients are not routinely screened for their psychological health. We sought to introduce regular mental health screening to all gastroenterology outpatient clinics at Royal Devon and Exeter (RD&E) and North Devon District hospital (NDDH) using the General Anxiety Disorder- 2 (GAD-2) and Patient Health Questionnaire-2 (PHQ-2).

Aims & Methods: Using QI methodology with Plan Do Study Act cycles (PDSA), a screening questionnaire was first trialled in gastroenterological outpatient clinics. Functionality and effectiveness of this screening tool was assessed and the GAD-2 and PHQ-2 scores of >2 were used to trigger referrals to talking therapy service called TalkWorks. Throughout each cycle data was collected on age, diagnosis and GAD-2, PHQ-2 scoring.

PDSA cycle 1: (24/8/18 - 19/9/18). At RD&E the questionnaire was handed out in the clinic waiting room. The ease and functionality of the questionnaire was assessed. Feedback was obtained from patients and service providers. PDSA cycle 2: (24/9/18- 6/11/18). The 2nd updated version was trialled again and no further alterations were made.

PDSA cycle 3: (11/3/19- 24/04/19). The 3rd version was sent out alongside a clinic appointment letter to every patient.

PDSA cycle 4: (08/11/2019- 27/11/2019). The questionnaire was trialled in a different hospital (NDDH) before being sent out to patients alongside clinic appointment letters.

Results: Across 4 cycles, data was collected from 287 (78:82:95:32) patient questionnaires. The mean age is 50.72. 55.4% (159/287) were female, 44.6% (128/287) were male. The rates of anxiety and depression were 20.6% (59/287) and 23.7% (68/287) respectively. 31.7% (91/287) had anxiety and/or depression. Higher scores were seen in females, with 37.7% (60/139) scoring for anxiety and/or depression than males 24.2% (31/128), $P = .02$. Patients with ulcerative colitis (77) and Crohn's disease (79) had similar rates of anxiety and/or depression, 26.0% (20/77) and 26.6% (21/79) respectively. Rates were non-significantly higher in the irritable bowel syndrome cohort (40), at 37.5% (15/40), $P = .51$.

Conclusion: In keeping with previous studies, we found a high prevalence of anxiety and depression in the gastroenterology clinic. A questionnaire incorporating GAD-2 and PHQ-2 is an effective and easy to administer tool to screen for psychological comorbidity amenable to talking therapies. Across RD&E and NDDH all gastroenterology patients are now being screened for anxiety and depression. Those identified are referred to an integrated psychological health service if appropriate. We aim to gather referral and outcome data from Talkworks to assess if the introduction of this screening has an impact on quality of life.

Disclosure: Nothing to disclose

Poster presentations *H. pylori*

H. pylori

09:00-19:00 / Poster Exhibition

P0204

PREVALENCE OF *HELICOBACTER PYLORI* DECREASED SIGNIFICANTLY DURING THE LAST 25 YEARS AMONG LITHUANIAN MEDICAL STUDENTS

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Introduction: The prevalence of *Helicobacter pylori* infection is decreasing in the modern Western world while remaining high in developing countries. There is limited up-to-date information about the prevalence of *H. pylori* in Eastern Europe.

Aims & Methods: The study was approved by the Bioethics Center of LUHS (no. BEC-MF-164). The groups of students from the 1st to the 4th study year were randomly selected in the Medical and Nursing Faculties. The students were tested for the presence of antibodies against *H. pylori* performing serological test from finger blood. Similar studies on the prevalence of *H. pylori* among LUHS students were performed in 1995, 2012 and 2016 by other authors. In 1995, the "Helisal" test was used, in 2012, 2016 and 2020 the "SureScreen Diagnostics Ltd" test was used.

Results: In the present study, 148 students of LUHS were examined. There were 120 female (81.1%) and 28 male (19.9%) students. The mean age of study participants was 20.4±1.7 years (min. 18 years, max. 33 years). The serological test for the presence of antibodies against *H. pylori* was positive in 21 (14.2%) students, negative in 125 (84.4%) students and 2 (1.4%) tests were non-informative. Non-informative tests were eliminated in further statistical analysis. *H. pylori* were found in 19 (16.1%) female students and in 2 (7.1%) male students. No significant difference between genders was observed ($p>0.05$).

The number of students who participated in the previous studies were: 120 in the year 1995 (mean age - 21.3±1.0 years), 187 in the year 2012 (mean age - 22.4±0.7 years), and 262 in the year 2016 (mean age - 20.4±1.0 years). *H. pylori* test was positive in 62 students (51.7%) in 1995, in 57 students (30.4%) in 2012, and in 69 students (26.3%) in 2016. The statistically significant difference in the prevalence of *H. pylori* was found between all study years, except between 2012 and 2016.

Conclusion: 1. In our study, *Helicobacter pylori* were established in 14.2% of students of Lithuanian University of Health Sciences.

2. Over the last 25 years, the prevalence of *H. pylori* among students of Lithuanian University of Health Sciences has decreased significantly.

References: 1. Roberts SE, Morrison-Rees S, Samuel DG, Thorne K, Akbari A, Williams JG. Review article: the prevalence of *Helicobacter pylori* and the incidence of gastric cancer across Europe. *Aliment Pharmacol Ther.* 2016 Feb 1;43(3):334-45. 2. Leja M, Grinberga-Derica I, Bilgiler C, Steininger C. Review: Epidemiology of *Helicobacter pylori* infection. *Helicobacter.* 2019 Sep 4;24(S1).

Disclosure: Nothing to disclose

P0205

STABLE RATE OF *HELICOBACTER PYLORI* INFECTION IN PATIENTS WITH PEPTIC ULCER DISEASE IN A TERTIARY REFERRAL HOSPITAL OVER THE LAST DECADE

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Introduction: *Helicobacter pylori* is a gastric luminal dwelling gram-negative bacterium associated with an increased risk of peptic ulcer disease and gastric cancer. A systematic review over two time periods (1970-1999 and 2000-2016) demonstrated declining trends in Europe (48.8% to 39.8%), Northern American (42.7% to 26.6%) and Oceania (26.6% to 18.7%) and static rates in Asia, Latin America and the Caribbean. Declining prevalence of infection in Europe is thought to have resulted from rising standards of living and improved sanitation. Proportionally more gastric and duodenal ulcers have been attributed to other causes such as medication and ischaemia.

Aims & Methods: Our aim was to assess year on year the proportion of patients diagnosed with gastric and duodenal ulcer in whom *H. pylori* was present. We interrogated our endoscopy database, for the period 01/01/2011 to 12/04/2020, returning a total of 999 oesophagogastrroduodenoscopies (OGDs) coded with a finding of gastric (522) and duodenal (477) ulcer. Presence of *H. pylori* was detected by observation on histology.

Helicobacter positivity rates over time were depicted graphically and a line of best fit was applied.

A "split point" year, following Hooi *et al* (2017), was selected which divided the timeline into two periods. An odds ratio for *Helicobacter* positivity in the later period, relative to the earlier, was calculated. This process was repeated with each of the years 2012 to 2020 serving as a split point.

Similar analysis was conducted using a probit regression model. *Helicobacter* positivity was the binary dependent variable. An independent dummy variable was constructed which took the value of 1 for investigations occurring in the later period.

Results: 21% (range 13% to 29% by year) of gastric ulcers and 31% (range 20% to 45% by year) of duodenal ulcers identified on endoscopy were *Helicobacter* positive. Graphical analysis of positivity rates over time show stable rates of *H. pylori* among patients with gastric ulcer and a small trend towards decreased prevalence in duodenal ulcer not meeting statistical significance. The odds ratio of *Helicobacter pylori* positivity in later periods, relative to earlier, was not significantly different from one for any of the analysed permutations.

Multiple probit regressions failed to demonstrate a significant relationship between time period and the probability of *Helicobacter* positivity.

Conclusion: This study fails to demonstrate a significant declining trend in *Helicobacter* infection associated with upper GI ulcers. *H. pylori* is still a very significant aetiology of upper GI ulcers with a significant associated morbidity and mortality.

References: Hooi, J. K. Y., et al. 2017, 'Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis', *Gastroenterology*, vol. 153, no. 2, pp. 420-429.

Disclosure: Nothing to disclose

P0206

HELICOBACTER PYLORI SCREENING IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Introduction: Potent antithrombotic therapy has significantly improved prognosis for patients with acute myocardial infarction (MI), however, at a price of increased bleeding risk. Chronic gastric infection with *Helicobacter pylori* (HP) commonly causes upper gastrointestinal bleeding (UGIB) and is proposed as a risk factor for MI. The prevalence of Hp in a current MI population and the feasibility of Hp screening as part of routine clinical care are unclear.

Aims & Methods: In this multicenter, open-label, clinical trial, all patients admitted for acute MI during the study period were eligible for enrollment. After written informed consent patients were tested for Hp infection with a bedside urea breath test (UBT [Mayoly Spindler]) incorporated into routine care during the hospitalization period.

Results: 274 consecutive MI patients (median age 67 years, 24% women) were enrolled. Overall, the HP prevalence was 20% (95% CI, 15.5-25.3). The proportion of proton pump inhibitors (PPI) users was significantly higher in Hp negative compared to Hp positive patients (38% vs. 16%; $P=0.003$). After censoring of the 93 subjects with PPI exposure preceding the UBT, the HP prevalence was 25%. After adjusting for age and sex, smoking was found to be significantly associated with testing positive compared with negative for HP (33% vs 20%, $P=0.03$).

Conclusion: Hp is highly prevalent in a contemporary MI population. Hp screening in the setting of acute MI was found to be feasible. A future randomized trial is needed to determine if routine Hp screening and subsequent eradication therapy improves bleeding complications, cardiovascular outcomes, and ultimately, prognosis.

Disclosure: Mayoly Spindler generously supported the diagnostics in this study, but had no role in the design of this study, data collection or interpretation of results.

P0207

CLARITHROMYCIN RESISTANCE IS MORE COMMON AMONG LESS VIRULENT *HELICOBACTER PYLORI* STRAINS - DATA FROM AN IRISH CENTRE

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Introduction: *H. pylori* can cause a range of pathologies, including chronic gastritis, peptic ulcers, gastric carcinoma and mucosa-associated lymphoid tissue lymphoma. Eradication is recommended in symptomatic patients, but increasing antibiotic resistance is making eradication progressively difficult. Patients are often treated with a first-line triple therapy containing a proton pump inhibitor, clarithromycin and amoxicillin. If first-line treatment fails, patients are frequently treated with a levofloxacin-based second-line therapy.

There is a high level of genetic diversity among *H. pylori* strains. Virulence factor genotypes are known to play a role in determining the severity of disease. The vacuolating cytotoxin A (VacA), which induces vacuole formation and the cytotoxin-associated gene A (CagA), which is injected into the host cells by a type IV secretion system and influences cell signalling, are two of the most studied virulence factors. Others include the adherence protein outer inflammatory protein A (OipA) and cytotoxin-associated gene E (CagE).

Aims & Methods: To evaluate correlations between *H. pylori* clarithromycin and fluoroquinolone resistance and virulence factor genotype.

DNA was isolated from combined antral and corpus biopsies of rapid urease test-positive endoscopy patients attending Tallaght University Hospital, Dublin. The GenoType HelicoDR assay (Hain Lifesciences) was used to detect resistance-mediating mutations. Genotyping for virulence factors was done by PCR. SPSS Statistics software (version 26) was used to perform chi-squared tests to analyse the correlations between the *H. pylori* virulence factor genotypes and antibiotic resistance. A p-value of < 0.05 was considered statistically significant.

Results: In all, 127 patients (mean age 48.3 ± 15.7 years; 59% (n=75/127) male) were included in the study, regardless of *H. pylori* treatment history. The most common histological finding was chronic gastritis (74%; n=94/127). Overall resistance to clarithromycin was 54.3% (n=69/127) and overall resistance to fluoroquinolones was 11.8% (n=15/127).

30.7% (n=39/127) of strains were *cagA*-positive. 60.6% (77/127) of strains had the S1/M2 *vacA* allele combination while 23.6% (n=30/127) had S1/M1, 15% (n=19/127) had S2/M2 and 0.8% (n=1/127) had S2/M1. 52.7% (n=67/127) of strains were *cagE*-positive and 56.7% (n=72/127) were *oipA*-positive.

Clarithromycin resistance was significantly lower in *cagA*-positive than *cagA*-negative strains (38.5% vs 61.4%, respectively: $\chi^2 = 5.7$, $p = 0.02$). Similarly, fewer *cagE*-positive strains were clarithromycin resistant than *cagE*-negative strains (44.8% vs 65%, respectively: $\chi^2 = 5.2$, $p = 0.02$). Clarithromycin resistance was also lower among more virulent *vacA* S1 genotypes compared to S2 (49.5% vs 80%, respectively: $\chi^2 = 6.3$, $p = 0.01$). No significant associations were found between *oipA* genotype and clarithromycin resistance or any of the virulence factor genotypes and fluoroquinolone resistance.

Conclusion: The absence of *cagA*, *cagE* and the presence of less virulent *vacA* genotypes are associated with clarithromycin resistance in this cohort. Although antibiotic resistance is increasing, clarithromycin resistance appears to be associated with less virulent strains of *H. pylori*.

Disclosure: Nothing to disclose

P0208

GENOTYPIC PRIMARY RESISTANCE TO CLARITHROMYCIN AND LEVOFLOXACIN DETECTED IN STOOL SAMPLES WITHIN A THREE YEAR PERIOD

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Introduction: Clarithromycin and levofloxacin are two antibiotics that are commonly used to treat *Helicobacter pylori* (*H. pylori*) infection. However, the rate of antibiotic resistance is the main reason for therapy failure, and depends on point mutations in bacterial DNA. Bacterial DNA in stools may

be used to detect such mutations in a non invasive way. We aimed to report the trend of *H. pylori* antimicrobial genotypic resistance in a three-year period, detected in fecal samples.

Aims & Methods: We enrolled consecutive people ≥ 18 years without previous diagnosis of *H. pylori* infection, referred for dyspepsia in the period 2017-19. Diagnosis of infection was achieved by concordance of histology and at least one non invasive test (either urea breath test or stool antigen).

Participants collected stool samples shortly after enrollment to be examined using a new fecal investigation (THD fecal test). A2142C, A2142G and A2143G point mutations in the 23S rRNA subunit gene for clarithromycin resistance, and C261A, C261G, G271A, A272G, G271T and A270T point mutations in the A-subunit of gyrase gene for levofloxacin resistance were assessed in stools by real time polymerase chain reaction (RT-PCR).

Results: Ninety-nine consecutive, *H. pylori* positive patients were enrolled (40 in 2017, 30 in 2018 and 29 in 2019). Resistance to clarithromycin was 30% in 2017, 30% in 2018 and 24.1% in 2019. Resistance to levofloxacin got ahead of 10% in 2017, 3.3% in 2018 and 34.5% in 2019. Double resistance was 5% in 2017, 3.3% in 2018 and 10.3% in 2019.

Conclusion: In the 3-year period in object, resistance to clarithromycin remained stable but above the critical threshold of 20%. On the other hand, we found a relevant peak in levofloxacin resistance in 2019 presumably due to the cross resistances among fluoroquinolones.

Disclosure: A. Di Leo served as consultant for T.H.D. spa

P0209

IMPACT OF *HELICOBACTER PYLORI* INFECTION ON SEVERITY OF METABOLIC SYNDROME-RELATED NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Nonalcoholic fatty liver disease (NAFLD) consists a novel major global burden, especially in West, and *Helicobacter pylori* infection (*Hp*-I) has been suggested as a risk factor for NAFLD, through insulin resistance (IR) and metabolic syndrome (MetS), although discrepancy exists.

This study aimed to investigate retrospectively any potential effect of active *Hp*-I on NAFLD severity in morbidly obese patients, subjected to bariatric surgery and gastric biopsy for documentation of *Hp*-I.

Aims & Methods: A total of 94304 patient-cases presented to the emergency department (ED) of Inselspital Bern from 1 January 2017 to 30 November 2018 were evaluated retrospectively for eligibility. Eligible were morbidly obese, adult patients underwent bariatric surgery and liver and gastric biopsy for documentation of NAFLD and active *Hp*-I, respectively.

Grading and staging of NAFLD was based on NASH Clinical Research Network scoring systems; for the discrimination between NAFL and NASH, both NAFLD, Activity Score and Fatty Liver Inhibition of Progression were used, the latter introduced in morbidly obese populations. Histologically severe disease was defined, as steatosis, activity and fibrosis (SAF) scoring system ≥ 3 and/or F ≥ 3 . Statistical analysis was performed with SPSS and significance was set at $p < 0.05$ (two tailed).

Results: Sixty-four patients were finally enrolled, with 15 having active *Hp*-I (23.4%). Higher rates of nonalcoholic steatohepatitis (NASH) were revealed to them than those without *Hp*-I (86.7% vs. 26.5%, respectively; $p < 0.001$). Histologically, steatosis grade ($p = 0.027$), ballooning ($p < 0.001$), lobular inflammation ($p = 0.003$) and fibrosis stage ($p < 0.001$) were also more severe in *Hp* infected patients. Likewise, liver function tests, and Mets parameters, like IR, dyslipidemia and arterial hypertension were significantly higher in *Hp* positive patients.

Conclusion: This study favors a potential impact of active *Hp*-I connected with Mets on NAFLD severity in morbidly obese patients underwent bariatric surgery and thus, further research is required.

Disclosure: Nothing to disclose

P0210

H.PYLORI INFECTION AND NUTRITIONAL STATUS IN END-STAGE RENAL DISEASE PATIENTS

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Introduction: End Stage Renal Disease (ESRD) patients have a high prevalence of malnutrition due to a protein-energy wasting. The pathogenic mechanism of this process is not completely defined, but it is possible that chronic *H. pylori* infection plays important role in it, possibly by causing dyspeptic symptoms, or even by decreasing the plasma levels of anabolic hormone, ghrelin.

Aims & Methods: The aim of this cross-sectional, single-center study is to investigate the prevalence of *H. pylori* infection in a population of ESRD patients, and it's possible influence on malnutrition development.

In a period between April 1, 2016 and March 1, 2020, a total of 178 ESRD patients without previous history of verified *H. pylori* infection, underwent upper endoscopy with multiple mucosal biopsies as a part of pre-kidney-transplantation assessment. Before endoscopic procedures, patients were interviewed for their dyspeptic symptoms using Gastrointestinal Symptom Rating Scale (GSRS), underwent body composition measurement, and their blood levels of pepsinogen I and II, as well as acyl-ghrelin were determined. Multiple regression analysis was used to study possible impact of *H. pylori* infection on development of dyspepsia, histological features of gastric atrophy, plasma levels of pepsinogen and ghrelin and clinical features of malnutrition.

Results: The prevalence of *H. pylori* infection in our ESRD patient population was 38.2% (68/178), significantly lower than predicted by our national *H. pylori* prevalence (88.3%). By using GSRS, we found that *H. pylori* positive patients did not complain on dyspeptic symptoms more often, even though histological analysis showed that the presence of infection significantly increased the risk of atrophic body gastritis (OR 2.4, CI 1.3-4.8, $p = 0.037$). We also found that the presence of histological features of gastric atrophy negatively correlated with acyl-ghrelin levels (29.6 vs 34.1 fmol/L; $P = 0.021$) as well as nutritional markers, such as pre-dialysis albumin levels (32.7 vs 39.2 g/L; $P = 0.028$) and body cell mass (33.0 vs 38.7%; $P = 0.035$).

Conclusion: Our population of ESRD patients had lower prevalence of *H.pylori* infection, but it significantly increased the risk of atrophic gastritis development. The possible clinical implication is that we must think of *H.pylori* eradication before progression to gastric atrophy in population of ESRD patients, in order to improve their prognosis and possibly quality of life.

Disclosure: Nothing to disclose

P0211

APPLICATION OF OLGA AND OLGIM STAGING SYSTEMS IN HP GASTRITIS

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Introduction: *H. pylori* infection is strongly associated with chronic gastritis and is probably the main cause of chronic inflammation in the gastric mucosa. Gradually, HP gastritis will result in gastric atrophy (GA) and intestinal metaplasia (IM), the two detectable precursor lesions in gastric carcinomas. Early endoscopic examination is of paramount importance in the early detection and treatment of advanced precursor lesions and cancer.

Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) are adopted to individualize the case with high evolutionary risk.

Aims & Methods: The aim of our study was to evaluate OLGA and OLGIM staging system in HP gastritis and to determine any correlations between these classifications.

One hundred and forty nine patients who underwent upper-endoscopy were enrolled into our study retrospectively from January 2019 to June 2019. The diagnosis of HP gastritis was confirmed by histologic examination. Epidemiological, endoscopic and anathomopathological data were collected. OLGA and OLGIM systems were applied to classify our patients according to cancer risk (stages 0-II are associated with low risk, while stages III and IV with high risk).

Results: Mean age was 51,27 years, the sex ratio 0.88. Upper endoscopy was epigastric pain in 60%, anemia in 18%, vomiting in 10,5 % and diarrhea in 6%. Endoscopic findings included antral gastropathy in 63%, fundic gastropathy in 20% and ulcers in 22%. According to histologic examination, HP density was mild in 28,8%, moderate in 34,2% and marked in 36%. Gastric atrophy was noted in 20,7%. It was mild in 64,5% and moderate in 22,5%. Six patients had severe GA and according to OLGA staging system low risk gastritis represented 95,2% and high risk gastritis were 4,8%. Intestinal metaplasia was noted in 16,7%. It was mild in 52%, moderate in 24% and six patients had severe IM.

According to OLGIM staging system, low risk gastritis represented 94,6% and high risk represented 5,4%. There was no significant association between the OLGA and OLGIM stages and the HP density ($p=0,2$ and $p=0,42$ respectively). However, low risk gastritis in OLGA staging system were significantly associated with marked HP density ($p=0,017$) and high risk gastritis were associated with mild HP density ($p=0,016$).

The association between OLGA staging system and the degree of intestinal metaplasia was significant ($p<0,001$) as well as the association between OLGIM staging system and the degree of gastric atrophy ($p<0,001$). According to both OLGIM and OLGA staging system, 91,5% patients had low risk gastritis and 5,2% had high risk gastritis with a positive correlation between the two systems ($p<0,001$). Discrepancies were noted in five cases.

Conclusion: OLGA and OLGIM staging systems can be very useful in evaluating gastric cancer risk. This correlation implies that close and frequent monitoring of high-risk patients is necessary to facilitate early diagnosis of gastric cancer.

Disclosure: Nothing to disclose

P0212

ENDOSCOPIC YIELD OF CHRONIC EPIGASTRIC PAIN SYNDROME IN OUTPATIENTS

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Introduction: The diagnostic evaluation and management of patients with chronic epigastric pain syndrome may differ geographically according to patient age, prevalence of *Helicobacter pylori*, and risk of gastric cancer. Guidelines recommend early endoscopy in dyspeptic patients who are older than 45 years, or present alarm features.

Aims & Methods: The aim of our study was to determine the prevalence of *H. pylori* and the performance characteristics of alarm features in predicting organic lesions.

A retrospective study of 91 patients with chronic epigastric pain who underwent upper endoscopy from January To June 2020 was conducted. Clinical characteristics, *H. pylori* prevalence, endoscopic and histological findings of patients with functional or organic causes of dyspepsia were compared. Organic lesions are defined by the presence of ulcers (defined as mucosal break of 3 mm or greater) or cancer (confirmed by histology). Alarm features are recent onset dyspepsia in a person > 45 years, odynophagia, progressive dysphagia, upper gastrointestinal bleeding, recurrent vomiting, unexplained weight loss. SPSS version 22.0 was used for the descriptive and comparative analyses.

Results: Mean age was 49.71 (± 16.5) years, 43.9% were male. Common alarm features were recent onset dyspepsia in a patient over 45 years in 62%, recurrent vomiting in 10.9% and anemia in 6.5%. The most frequent endoscopic finding was antral gastropathy in 59.8%. The major organic lesions were gastric or duodenal ulcers (21,7%). No malignancies were noted. Twenty one patients had normal esophagogastroduodenoscopy (EGD) (23,07%). The prevalence of *H. Pylori* was 64%. Of patients with organic lesions, 70% were *H. pylori*-positive.

In univariate analysis, only age older than 45 years was associated with organic lesions ($p=0,05$). The pooled sensitivity and specificity of any alarm feature for organic lesions were 80% and 63%, the PPV and NPV were 26,2% and 86,7% respectively.

Conclusion: In our experience, most of chronic epigastric pain syndrome were diagnosed with functional or *H. pylori*-associated syndrome. The presence of alarm features was not sensitive or specific for differentiating organic and functional dyspepsia.

Disclosure: Nothing to disclose

P0213

NRF2 ROLE AND TARGETING IN *HELICOBACTER PYLORI*-INDUCED GASTRIC CARCINOGENESIS

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Introduction: Gastric cancer (GC) is the third leading cause of cancer death worldwide and is responsible of many relapse cases. Chronic infection with *Helicobacter pylori* is the major risk factor of GC through induction of chronic inflammation and oxidative stress. Our team has participated to the demonstration that *H. pylori* infection leads to the emergence of cells having cancer stem cells (CSC) properties through an epithelial to mesenchymal transition (EMT). The transcription factor Nrf2 is the major driver of cellular antioxidant response activated after a high oxidative stress. In addition, Nrf2 expression has been correlated to gastric cancer progression and is higher in cancer stem cells.

Aims & Methods: The aims of the project are: (i) to check the activation of Nrf2 signaling pathway after *H. pylori* infection, (ii) to decipher the role of Nrf2 in EMT and CSC emergence and (iii) to target the pathway using polyphenols which are natural modulators of Nrf2.

Results: Kinetic infection of AGS and MKN74 cells with *H. pylori* induces an early activation of Nrf2 signaling pathway shown by increase of nuclear translocation of Nrf2, by activation of the antioxidant responsive element (ARE) sequence and by increase expression of target genes and proteins such as GSH, HO-1, SOD, catalase, TRX. Inhibition of Nrf2 by CRISPR-Cas9 strategy leads to an increase of EMT-related gene expression and to cells with CSC properties shown by tumorsphere assays. Transcriptomic analyses of patient-derived xenograft (PDX) cells, FACS-sorted for the CSC marker CD44, showed that CD44⁺ cells exhibit a higher Nrf2 signature than CD44⁻ cells. Moreover, polyphenols can be used to target Nrf2 and can be combined with classical chemotherapy agents to decrease the number of tumorsphere-forming cells.

Conclusion: In conclusion, infection with *H. pylori* induces an early activation of the Nrf2 signaling pathway. Our results demonstrate that Nrf2 is important for the maintenance of the epithelium integrity and the control of CSC emergence and is overactivated in CD44⁺ gastric PDX cells. Finally, it is possible to modulate Nrf2 using natural polyphenols to specifically target CSC.

Disclosure: Nothing to disclose

P0214

LUMINAL NITRIC OXIDE IS INCREASED IN *HELICOBACTER PYLORI*-INDUCED GASTRIC INFLAMMATION AND RELATED TO VIRULENCE FACTORS OF THE BACTERIUM

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Introduction: *Helicobacter pylori* (*H. pylori*) categorized as the major risk factor in the development of chronic gastritis, peptic ulcer disease and gastric cancer, is considered a major health threat worldwide. Nitric oxide (NO) has been shown to protect the gastric mucosa against damage and to stimulate repair and healing of mucosal inflammation, erosions and

ulcerations. In line with this, NO produced via inducible nitric oxide synthase might be elaborated in response to *Helicobacter pylori*-associated inflammation.

Aims & Methods: The present study was conducted to investigate the relationship between *H. pylori* infection, and gastric luminal NO levels with inflammatory-associated immunological and histopathological findings and the possible usefulness of NO measurements in the diagnostic setting.

In 96 consecutive adult patients (56 women, 40 men), who were referred to routine diagnostic upper gastrointestinal endoscopy after being diagnosed with *H. pylori* infection by the urea breath test (UBT). Immediately during upper endoscopy, luminal NO was measured by chemiluminescence, and two biopsies were obtained for culture, one from the gastric antrum and one from corpus. In addition, ELISA and immunoblot tests performed on blood samples.

Later, measured NO levels were correlated with the presence of *H. pylori*, the immune response to virulence factors of the bacteria, e.g. CagA, VacA, the ELISA optical density and histopathological grades for acute and chronic inflammation, atrophy, intestinal metaplasia and pseudopyloral metaplasia. In a subset of patients and controls a 40-plex cytokine/chemokine electrochemiluminescence assay was carried out in order to reveal possible inflammatory mediators in *Helicobacter* infection and NO release.

Results: *H. pylori*-positive patients had significantly higher luminal NO levels (336 ± 26 ppb) than *H. pylori*-negative (128 ± 47 ppb) ($p < 0.0001$). The *H. pylori*-positive with CagA-negative infection had slightly higher NO levels (390 ± 56 ppb) than the CagA-positive (321 ± 30 ppb) patients. No correlation was seen between the NO level and presence of VacA. Histopathological changes of the mucosa were found in almost all (99%) *H. pylori*-positive patients.

However, 37% of the *H. pylori*-negative patients displayed histopathological changes. High percentage 78-100% of histopathological concordance were found between the paired biopsies from the corpus and antrum, which displayed the same histological grade. A positive trend was found between the gastric luminal NO levels and the degree of acute inflammation. Similarly, a positive trend was noted between mean serum IgG ELISA optical density (OD) readings and degree of chronic inflammation. The grading of atrophy, intestinal metaplasia or pseudopyloral metaplasia did not correlate with the measured gastric NO levels.

Conclusion: Our study results show that luminal gastric NO is increased in *H. pylori*-infected patients due to the inflammatory response in the mucosa. Positive trends were found between the gastric luminal NO levels and the degree of acute inflammation in the mucosa, as well as the serum levels of anti-*H. pylori* IgG and CagA-positivity in the bacterial strains.

Disclosure: Nothing to disclose

P0215

"TEST-AND-TREAT" STRATEGY WITH UREA BREATH TEST: A COST-EFFECTIVE APPROACH FOR THE MANAGEMENT OF *HELICOBACTER PYLORI*-RELATED DYSPEPSIA AND THE PREVENTION OF PEPTIC ULCER IN THE UNITED KINGDOM - RESULTS OF THE HP-BREATH INITIATIVE

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Introduction: Clinical data comparing strategies used for the management of *H. pylori*-associated diseases are limited. In the UK, Stool Antigen Test (SAT) seems to be the most frequently used non-invasive test for *H. pylori* detection. Cost-effectiveness studies might help to identify optimal strategies.

Aims & Methods: To assess cost-effectiveness of the "Test-and-Treat" strategy with Urea Breath Test (UBT) versus other strategies, in patients with *H. pylori*-associated dyspepsia and peptic ulcer in the UK. Cost-effectiveness models compared four strategies: "Test-and-Treat" including either UBT or SAT, "Endoscopy and Treat" and "Symptomatic Treatment". Advanced simulations were performed over a 4 week time horizon for the endpoint "Probability of dyspepsia symptoms relief" and over 10 years for the "Probability of peptic ulcer avoided". Models were developed according to UK routine medical practice and costs.

Results: For the "Probability of dyspepsia symptoms relief" endpoint, "Test-and-Treat" strategies with either UBT or SAT were the most cost-effective (respectively 526€ and 518€/success) versus "Endoscopy and Treat" and "Symptomatic Treatment" (respectively 1,280€ and 1,029€/success). For the "Probability of peptic ulcer avoided" endpoint, "Test-and-Treat" strategies with either UBT or SAT were also the most cost-effective (respectively 208€ and 191€/peptic ulcer avoided/year) versus "Endoscopy and Treat" and "Symptomatic Treatment" (respectively 717€ and 651€/peptic ulcer avoided/year); (1 EUR = 0,871487 GBP).

Conclusion: "Test-and-Treat" strategies with either UBT or SAT are the most cost-effective medical approaches for the management of *H. pylori*-associated dyspepsia and the prevention of peptic ulcer in the UK. "Test-and-Treat" strategy with UBT has comparable cost-effectiveness outcomes to the strategy utilising SAT.

Disclosure: This study was funded by Mayoly Spindler Laboratories. DMP, JB, ILPB, PM have received honoraria from Mayoly Spindler Laboratories for their contribution to the study; HS is an employee of Mayoly Spindler Laboratories; AB has received honoraria from Mayoly Spindler Laboratories for data management and data analyses; PM has received honoraria for consultancy from Bayer, Danone and speaker honoraria from Alfasigma, Bayer, Dr Falk, Malesci.

P0216

PERSONALISED MEDICINE: IS THIS THE WAY TO COMBAT *HELICOBACTER PYLORI* (HP) ERADICATION FAILURE?

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Introduction: Antibiotic-resistant HP varies in different geographical areas. A recent review of international guidelines suggest evidence-based locally relevant treatment strategies. Within the United Kingdom, hospitals develop local antibiotic guidelines as per local resistance rates. However, Public Health England (PHE) recommendation for treatment regimes in primary care remains to be clarithromycin and metronidazole-based regimes for patients with dyspepsia who are HP positive. The Gastrointestinal Bacteria Reference Unit (GBRU), PHE is the national reference laboratory which tests all HP cultures in England. We aimed to look local HP secondary resistance data from 3 different units in London and compared whether variation in specimen collection practice impacted on rates of HP culture positivity.

Aims & Methods: We compared culture data from 3 different units in London. Due to differences in the local databases used, the date ranges of data collected was varied.

We obtained 34 months data between March 2016 and December 2018 from Homerton University Hospital (HUH). There were no local guidelines at HUH regarding number of biopsy samples taken and samples were transported to the lab routinely.

Culture data from Guys & St Thomas' Hospital (GST) was for 10 months between January to October 2019. At least 4 to 6 samples were taken on Monday to Thursday morning lists to ensure samples are sent to reference lab urgently.

Culture data from Newham University Hospital (NUH) was for 12 months from October 2018 to October 2019. At least 6 gastric biopsy samples were taken on a dedicated endoscopist's list on a weekday morning and samples were urgently transported by taxi to the laboratory.

Results: 122 gastric biopsy samples were sent in HUH and 36 isolated HP, giving a 29.5% positive culture rate.

112 gastric biopsy samples were sent in GST and 72 isolated HP, giving a 64.2% positive culture rate.

34 gastric biopsy samples were sent in NUH and 15 isolated HP, giving a 44.1% positive culture rate.

Phenotypic HP sensitivities by hospital:

Amoxicillin: HUH 100%, GST 100%, NUH 100%

Tetracycline: HUH 97%, GST 100%, NUH 100%

Levofloxacin: HUH 72%, GST 77%, NUH 53%

Metronidazole: HUH 4%, GST 20%, NUH 7%

Clarithromycin: HUH 28%, GST 39%, NUH 7%

Percentage of antibiotic resistance by hospital:

HUH - 22% single resistance, 56% dual resistance, 22% triple resistance

GST - 19% fully sensitive, 23% single resistance, 39% dual resistance, 19% triple resistance

NUH - 7% single resistance, 53% dual resistance, 40% triple resistance.

Conclusion: 38% of UK's foreign born population live in London. Variation in concentrations of migrant communities within a city can lead to variations in antimicrobial resistance. Our results are skewed towards resistant

isolates as patients having gastroscopy and cultures taken for HP sensitivity would have had multiple courses of antibiotics. They suggest a benefit in tailoring local second line antimicrobial guidelines to local resistance rates. Given the lack of amoxicillin resistance, we recommend penicillin allergy testing for patients who report allergy.

Disclosure: Nothing to disclose

P0217

ACCURACY OF THE *HELICOBACTER PYLORI* DIAGNOSTIC TESTS IN PATIENTS WITH PEPTIC ULCER BLEEDING- THE RESULTS OF A NETWORK META-ANALYSIS

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Introduction: Peptic ulcer (PU) being the most frequent source of gastrointestinal bleeding and *Helicobacter pylori* is a main etiologic factor for it. Some studies suggest accuracy of the diagnostic tests is decreased in PU bleeding. The international guidelines are vague on the method of testing in the setting of acute PU bleeding. However, detection of *H. pylori* would be essential as it reduces the risks of untoward outcomes.

Aims & Methods: Our aim was to update the most recent meta-analysis [1] which included studies until 2004 and to assess the accuracy of one or a combination of more diagnostic tests for *H. pylori* in patients with bleeding peptic ulcer.

A comprehensive literature search was carried out from inception to November 2019 to perform a network meta-analysis. We collected the raw data of diagnostic tests such as true positive, true negative, false positive and false negative values. All statistical calculations performed by R programming language using anova arm-based model by Nyaga et al., 2018. We ranked the methods index tests according to the superiority index and calculated pooled sensitivity and specificity.

Results: We analyzed 7 arbitrary gold standards in 7 networks against a single or a combination of diagnostic index tests. None of the calculated superiority indices proved that any of the tests have better diagnostic accuracy than the individual index tests.

Conclusion: The results from the network meta analysis showed that none of the current diagnostic tests for *H. pylori* are better or worse in the diagnosis of the infection in the context of PU bleeding.

References: Gisbert, J.P. and V. Abaira, Accuracy of *Helicobacter pylori* diagnostic tests in patients with bleeding peptic ulcer: a systematic review and meta-analysis. *Am J Gastroenterol*, 2006. 101(4): p. 848-63.

Disclosure: Nothing to disclose

P0218

MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION AT THE PRIMARY CARE LEVEL: EVALUATION OF DIFFERENT STRATEGIES TO IMPROVE ITS APPROACH

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Introduction: *Helicobacter pylori* (Hp) infection is now mainly managed at primary care level. Previously, our group showed that the strategy of sending specific counselling (SC) to primary care physicians (PCP), (a personal letter with accepted indications and treatment issued by their referent Gastroenterologist) has significantly improved treatment regimens and eradication rates, but not indications (1). New strategies in order to improve *Helicobacter Pylori* infection management are still needed.

Aims & Methods: To evaluate and compare the effect of formative lessons (FL) in primary care centers (PCC) in addition to sending specific counselling in urea breath test (UBT) indications, treatment regimens and eradication rates.

Firstly, we prospectively included 399 consecutive UBT indicated by PCP after sending a SC

(Phase I). Then, formative lessons were given in four PCC from our health area with high number of UBT requests. After that period, 400 consecutive UBT were prospectively included, 100 from PCC with FL and 300 from PCC without FL (Phase II). Specific counselling has been previously sent to both groups of PCC.

Appropriate UBT indications and treatment regimens were considered according to national guidelines and consensus documents.

Results: We have analyzed 799 UBT, 399 after sending SC and 400 after FL period (100 from PCC with FL and 300 from PCC without FL). The mean age was 47.33±15.68 years old, 64.7% were women. An improved trend is observed in appropriate indication between phase I group (SC sent) and PCC with FL (57.5% vs 67%; p=0.06). No differences were observed in appropriate indications between PCC with FL and without FL (67% vs 62.9% p=0.45). Appropriate treatment regimens were significantly higher in PCC with FL compared to phase I group (94% vs 75.3%; p=0.01). Also they were significantly higher in PCC with FL compared to PCC without FL (94% vs 85.6%; p=0.03). However, no differences in eradication rates were observed among groups.

Conclusion: The strategy of sending specific counselling to PCP has significantly improved treatment regimens and eradication rates but not indications. Formative lessons after sending a specific counselling improve indications and treatment regimens but no eradication rates.

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Disclosure: Nothing to disclose

P0219 WITHDRAWN

P0220

EFFICACY AND SAFETY OF MODIFIED BISMUTH QUADRUPLE THERAPY AND CONCOMITANT THERAPY FOR *HELICOBACTER PYLORI* INFECTION IN RAJAVITHI HOSPITAL: A RANDOMIZED CONTROLLED TRIAL

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Introduction: The failure rate of the standard triple therapy for *H. pylori* infection has been increasing due to the rising prevalence of antimicrobial resistance. Concomitant therapy has been recommended to replace the standard triple therapy in regions with high rate of clarithromycin resistance. Since bismuth has shown its effectiveness to increase the eradication rate of *H. pylori* infection with lower treatment-related side effects, this study was, therefore, conducted to compare the efficacy and safety of *H. pylori* eradication using the triple bismuth therapy and standard concomitant therapy.

Aims & Methods: This study was conducted to i) compare the *H. pylori* eradication rates in patients treated with different treatment interventions (10-day modified triple bismuth therapy and 10-day standard concomitant therapy) and ii) assess the treatment-related side effects between the treatment regimens.

Materials and methods: A total of 205 patients who underwent upper gastrointestinal endoscopy at Rajavithi Hospital, Bangkok between January 2018 and November 2018 and were diagnosed with *H. pylori* infection were included. Considering the exclusion criteria of severe comorbidities, previous *H. pylori* treatment, history of antibiotic ingestion, and penicillin allergy, 173 active *H. pylori* infected patients were randomized (1:1) and allocated into either the 10-day modified triple bismuth therapy (omeprazole 20 mg b.i.d., amoxicillin 1000 mg b.i.d., clarithromycin 500 mg b.i.d. and bismuth subsalicylate 1048 mg b.i.d.) or the 10-day standard concomitant therapy (omeprazole 20 mg b.i.d., amoxicillin 1000 mg b.i.d., clarithromycin 500 mg b.i.d. and metronidazole 400 mg t.i.d.). Four weeks after the completion of treatment, the ¹⁴C-urea breath test was performed to evaluate the *H. pylori* eradication rate. The efficacies of treatments were analyzed using the intention-to-treat (ITT) and per-protocol (PP) analyses. The safety of treatment was evaluated by using the records of the treatment-related symptoms and side effects and patients' compliance.

Results: A total of 86 and 87 *H. pylori* infected patients were randomly allocated into the 10-day modified triple bismuth therapy and standard concomitant therapy, respectively. The eradication rates of the modified triple bismuth therapy were 87.2% for ITT and 92.6% for PP. While the eradication rates of the standard concomitant therapy were 87.4% for ITT and 92.7% for PP. The common mild side effects of both regimens which were bitter taste, nausea, dizziness, and vomiting were less commonly reported in the modified triple bismuth group. Bitter taste was the most common side effect of both treatment regimens with the incidence of 13.6% in the modified triple bismuth group and 25.6% in the standard concomitant group. Two patients of the standard concomitant group experienced severe nausea/vomiting, headache and dizziness after the treatment.

Conclusion: The *H. pylori* treatment using the 10-day modified triple bismuth therapy achieved the acceptable eradication rate with fewer side effects, as compared to the standard 10-day concomitant therapy. This regimen can be considered as a good alternative *H. pylori* treatment in Thailand.

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Disclosure: Nothing to disclose

P0221

RANDOMIZED CLINICAL TRIAL COMPARING TRIPLE THERAPY VERSUS NON-BISMUTH BASED QUADRUPLE THERAPY FOR ERADICATION OF *HELICOBACTER PYLORI* IN KUWAIT

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Introduction: *Helicobacter pylori* (*H. pylori*) induced chronic infection is associated with peptic ulcer, chronic gastritis, gastric cancer, and increasing antibiotic resistance. Eradication of *H. pylori* reduces morbidity in patients with chronic gastritis and can prevent gastric cancer in the high-risk population.

Aims & Methods: We aimed to evaluate the efficacy of clarithromycin-based triple therapy and non-bismuth based quadruple therapy for eradicating *H. pylori* in patients with chronic gastritis in Kuwait. We enrolled a total of 606 treatment-naïve dyspeptic patients with gastric biopsy-proven chronic gastritis secondary to *H. pylori* in a prospective, open-label, randomized study conducted at the gastroenterology outpatient clinics of Haya Al-Habeeb gastroenterology center in Kuwait. Patients were randomized into two groups: the first group received the standard triple therapy (omeprazole, amoxicillin, and clarithromycin) for 14 days; and the second group received quadruple therapy (omeprazole, amoxicillin, clarithromycin, and metronidazole) for 14 days. All patients were tested for the eradication of *H. pylori* by carbon-13 urea breath test (13 C-UBT) one month after completion of eradication therapy.

Results: The overall eradication rate in both groups was 63.18%. The eradication rates in intention to treat (ITT) and per protocol (PP) population were 58.4% and 64.6%, respectively in triple therapy group. While in the quadruple therapy group, the eradication rates in ITT and PP population were 68% and 78.5%, respectively with a statistically significant higher eradication rate in patients treated by quadruple therapy than the triple therapy ($P > 0.01$). Multivariate logistic regression analysis showed that treatment regimen was the only significant predictor for successful *H. pylori* eradication (OR 1.98, 95% CI [1.3 to 2.9]); $P = 0.001$). The most common adverse events were abnormal taste, headache, dizziness, and abdominal pain.

Conclusion: Non-bismuth based quadruple therapy is more effective than slandered clarithromycin-based triple therapy for eradicating *H. pylori* in patients with chronic gastritis in Kuwait.

Disclosure: Nothing to disclose

P0222

RIFABUTIN TRIPLE THERAPY FOR FIRST-LINE AND RESCUE TREATMENT OF *HELICOBACTER PYLORI* INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Due to the increasing resistance of *H. pylori* there is a need for novel antibiotic treatment protocols.

Aims & Methods: We aimed to perform a meta-analysis of clinical trials in order to determine the effectiveness and safety of rifabutin triple therapy for *H. pylori* infection. We selected prospective clinical trials with a treatment arm consisting of proton pump inhibitor, amoxicillin and rifabutin, and a recorded outcome measure.

Results: Thirty-three studies including 44 data sets were included. The pooled eradication success for rifabutin triple therapy was 73.2% (95% CI 0.710-0.753) and the pooled OR for rifabutin triple therapy vs control was 1.40 (95% CI 1.103-1.775, $I^2=73.55$, $p=0.006$). Treatment was more likely to be successful when given first line vs rescue (82.4% vs 71.3%, $p=0.0001$), in Asian vs non-Asian populations (81.0% vs 72.4% $p=0.001$) and when drug dose or duration were augmented (80.6% vs 66.0% $p=0.0001$). The overall event rate for adverse effects was 25.3% (95% CI 0.23-0.28) and the pooled OR for adverse effects in the treatment vs control group was 0.79 (95% CI 0.57-1.09, $I^2=61.58$, $p=0.15$).

Conclusion: Rifabutin is a relatively safe and effective option for first-line and rescue treatment for *H. pylori* infection in adults.

Disclosure: Nothing to disclose

P0223

PCAB-BASED *HELICOBACTER PYLORI* ERADICATION IN PATIENTS WITH PENICILLIN ALLERGY

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Introduction: Recently, the potassium-Competitive Acid Blocker, Vonoprazan, has been increasingly used for *Helicobacter pylori* eradication in Japan, and a meta-analysis has demonstrated a higher eradication rate using a vonoprazan-containing regimen combined with amoxicillin and clarithromycin than PPI based regimen. Of all patients, 3-7% are allergic to penicillin. In cases of penicillin allergy, it is necessary to develop a new regimen without amoxicillin, and clarithromycin, metronidazole, and sitafloxacin currently represent the major antibiotics for *H. pylori* eradication therapy in Japan.

Aims & Methods: To reveal the effectiveness and safety of first-line therapy with vonoprazan, clarithromycin, and metronidazole, and second-line therapy with vonoprazan, metronidazole, and sitafloxacin for *H. pylori* infected patients with penicillin allergy. This interventional single arm study was registered as jRCTs031180133. The treatment regimens were vonoprazan 20mg bid, clarithromycin 200mg or 400mg bid, and metronidazole 250mg bid 7days for first-line therapy, and vonoprazan 20mg bid, metronidazole 250mg bid, and sitafloxacin 100mg bid 7days for second-line. Eradication success was assessed by the urea breath test.

Results: Sixty cases were enrolled. The average age of the patients was 65 years old. Seventeen males and 43 females were included. The first patient was included in March 2015, and about 15 patients per year

were included thereafter. The last patient was included in August 2019. Forty-three and 17 cases underwent first-line or second-line eradication therapy, respectively. The eradication rate of first-line therapy with vonoprazan, clarithromycin and metronidazole for 7-days was 92.9% (95%CI: 80.5-98.5%, $n=42$), and the eradication rate of second-line therapy with vonoprazan, metronidazole and sitafloxacin for 7-days was 88.2% (95%CI: 63.6-98.5%, $n=17$). One patient in whom *H. pylori* was eradicated with first-line therapy was excluded from analysis, because the urea breath test was not performed after the eradication. In all 60 cases, drug compliance was good, and no serious adverse events were reported.

Conclusion: First-line 7-day therapy with vonoprazan, clarithromycin and metronidazole, and second-line 7-day therapy with vonoprazan, metronidazole and sitafloxacin showed sufficient efficacy and safety for *H. pylori* infected patients with penicillin allergy.

Disclosure: Nothing to disclose

P0224

PHASE 3 STUDY EVALUATING THE EFFICACY AND SAFETY OF VONOPRAZAN 20 MG VERSUS LANSOPRAZOLE 30 MG IN THE TREATMENT OF ENDOSCOPICALLY CONFIRMED DUODENAL ULCERS IN ASIAN SUBJECTS WITH OR WITHOUT *HELICOBACTER PYLORI* INFECTION

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Introduction: Duodenal ulcers (DU) are a growing health concern in Asia. Proton-pump inhibitors such as lansoprazole are the first-line therapy for DU. Vonoprazan, a potassium-competitive acid blocker, has shown superior healing compared with lansoprazole in Japanese patients with erosive esophagitis; however, lack of sufficient clinical data for use of vonoprazan in Asian patients with DU.

Aims & Methods: This study, evaluated the efficacy and safety of vonoprazan versus lansoprazole in the treatment of DU in Asian patients. In this phase 3, multicentre, double-blind, double-dummy, non-inferiority, randomised study, Asian adults with endoscopic evidence of active DU ≥ 5 mm received oral vonoprazan 20 mg or lansoprazole 30 mg. The study drugs were given once daily, but *Helicobacter pylori* (*Hp*) + patients received the study drugs twice daily for the first 2 weeks as part of bismuth-containing quadruple *Hp* eradication therapy.

Primary end point was percentage of patients with endoscopically confirmed healing of DU, defined as disappearance of all white coats associated with DU, at week 4 or 6. Secondary end points included successful *Hp* eradication after 4 or 6 weeks, as determined by ¹³C urea breath test 4 weeks post-treatment and resolution of gastrointestinal (GI) symptoms associated with DU at weeks 2 to 6. The non-inferiority margins were -6% and -10% for the primary and *Hp* eradication end points using a 2-sided 95% confidence interval (CI).

Results: In total, 533 patients were randomised to receive either vonoprazan (n = 265) or lansoprazole (n = 268). Baseline characteristics were comparable between the groups. Majority (85.4%) of the patients were *Hp*+. The primary outcome of endoscopically confirmed healing of DU was observed in 96.9% and 96.5% of patients in the vonoprazan and lansoprazole groups, respectively (difference: 0.4%; 95% CI: -3.00%, 3.79%), thus meeting the primary end point of non-inferiority of vonoprazan versus lansoprazole. The lower limit of CI was above the non-inferiority margin of -6%. The secondary outcome of *Hp* eradication was seen in 91.5% and 86.8% of patients in the vonoprazan and lansoprazole groups, respectively (difference: 4.7%; 95% CI: -1.28%, 10.69%), showing non-inferiority of vonoprazan versus lansoprazole. No significant difference was observed in the percentage of subjects with post-treatment resolution of GI symptoms between the 2 groups. Treatment-emergent adverse event (TEAE) rates were 74.1% and 64.9% for vonoprazan and lansoprazole, respectively. The difference in TEAE rates was largely due to higher incidences of pepsinogen test positive (47.1% vs. 10.4%), pepsinogen I increased (35.0% vs. 13.8%) and abnormal gastrin test (36.9% vs. 7.5%) in the vonoprazan group compared with lansoprazole group, respectively. Treatment discontinuation rates due to TEAE were 1.5% (n = 4) and 2.2% (n = 6) in the vonoprazan and lansoprazole groups, respectively. Serious TEAE rates were similar between the groups (vonoprazan, 0.4%, n = 1; lansoprazole, 1.1%, n = 3), with no deaths reported in both the groups.

Conclusion: Vonoprazan was non-inferior to lansoprazole in healing DU and eradicating *Hp* in Asian patients. Vonoprazan was well tolerated and had a similar safety profile to lansoprazole.

Disclosure: The study was funded by Takeda Pharmaceutical Company Ltd. Liqun Gu and Chui Fung Chong are employees of Takeda Development Center Asia, Pte, Ltd, and Chui Fung Chong is the stock shareholder in Air Liquide and Abbott Laboratories. Ltd. Kentarou Kudou is an employee of Takeda Pharmaceutical Company Limited, Japan. Shutian Zhang, Xiaohua Hou, Fandong Meng, Jiangbin Wang, Weihong Sha, Cheng-Tang Chiu and Chung Woo Chul have no disclosures.

P0225

FIRST-LINE *H. PYLORI* ERADICATION THERAPY IN EUROPE: RESULTS FROM 24,882 CASES OF THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: The best approach for *Helicobacter pylori* management remains unclear. An audit process is essential to ensure clinical practice is aligned with best standards of care.

Aims & Methods: International multicentre prospective non-interventional registry starting in 2013 aimed to evaluate the decisions and outcomes in *H. pylori* management by European gastroenterologists. Patients were registered in an e-CRF by AEG-REDCap up to April 2020. *Variables included:* demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Modified intention-to-treat (mITT) and per-protocol (PP) analyses were performed and data were subject to quality review to ensure information reliability.

Results: In total 36,319 patients from 29 European countries were evaluated and 24,882 (70%) first-line empirical *H. pylori* treatments were included for analysis. Triple therapy with amoxicillin and clarithromycin was most commonly prescribed (40%), followed by concomitant treatment (19%) and bismuth quadruple (Pylera®) (10%) achieving 83%, 91% and 95% mITT eradication rate, respectively.

Over 90% effectiveness was obtained only with 10 and 14-day bismuth quadruple or 14-day concomitant treatment (Table). Longer treatment duration, higher acid inhibition and compliance were associated with higher eradication rates.

Conclusion: Management of *H. pylori* infection by European gastroenterologists is heterogeneous. Only quadruple therapies lasting at least ten days are able to achieve over 90% eradication rates.

Disclosure: Dr. Nyssen has received research funding from Mayoly, Allergan. Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Mayoly, Allergan, Diasorin.

First-line treatment	Length (days)	mITT, N (%)	(95% CI)	PP, N (%)	(95% CI)
Triple-C+A	7 / 10 / 14	1,903 (83) / 3,057 (83) / 72,264 (89)	(81-84) / (82-85) / (88-90)	1,886 (83) / 3,015 (84) / 2,238 (89)	(81-85) / (82-85) / (88-91)
Triple-A+M	7 / 10	118 (81) / 163 (85)	(74-89) / (79-90)	117 (81) / 161 (85)	(74-89) / (79-91)
Triple-C+M	7 / 10 / 14	724 (84) / 114 (65) / 80 (70)	(82-87) / (56-74) / (59-81)	721 (85) / 112 (66) / 80 (70)	(82-87) / (57-75) / (59-81)
Triple-A+L	7 / 10	178 (79) / 142 (85)	(72-85) / (79-91)	176 (78) / 136 (86)	(72-85) / (80-92)
Sequential-C+A+M/T	10	596 (83)	(80-86)	556 (85)	(82-88)
Quadruple-C+A+M/T	10 / 14	2,378 (88) / 2,228 (93)	(87-90) / (92-94)	2,316 (89) / 2,180 (93)	(88-90) / (92-94)
Quadruple-C+A+B	10 / 14	394 (86) / 1,194 (91)	(82-89) / (89-93)	390 (86) / 1,178 (91)	(83-90) / (90-93)
Quadruple-M+Tc+B	10	130 (94)	(89-98)	130 (94)	(89-98)
Pylera® (M+Tc+B)	10	2,267 (95)	(94-96)	2,223 (95.5)	(95-96)

[Table 1 Effectiveness (by modified intention-to-treat and per-protocol analyses) of first-line empirical treatments in Europe.]

mITT: modified intention-to-treat; PP: per-protocol; A - amoxicillin, C - clarithromycin; M - metronidazole; T - tinidazole; L - levofloxacin B; - bismuth salts; Tc - tetracycline.

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Introduction: Even with the currently most effective treatment regimens, approximately 10-20% of patients will fail to obtain *H. pylori* eradication.

Aims & Methods: To evaluate the effectiveness and safety of second-line empirical treatments in Europe.

A systematic prospective registry of the clinical practice of European gastroenterologists regarding *H. pylori* infection and treatment was established. All infected adult patients were systematically registered at AEG-REDCap e-CRF from June 2013 to April 2020. *Variables included:* Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Modified intention-to-treat (mITT) and per-protocol (PP) analyses were performed and data were subject to quality review.

Results: Overall, 5,516 patients from 29 countries were given a second-line therapy; from those, 4,862 (88%) were treated empirically and were therefore included for analysis. Mean age was of 49 (±15) years, 64% were

women and 5% had penicillin allergy. Most frequent treatment indications were dyspepsia (54%) and gastroduodenal ulcer (17%). Endoscopy was performed in 48% of the cases and ¹³C-UBT was used in 45% to diagnose the infection. Overall effectiveness was 83.7% (by mITT) and 84% (by PP). Over 97% of patients were compliant. AEs were reported in 28% of the cases and tolerance was similar among therapies. Most frequent second-line prescriptions and effectiveness per antibiotic combination is shown in table 1. After failure of first-line clarithromycin-containing treatment, optimal eradication (>90%) was obtained with moxifloxacin-containing triple therapy, the single capsule (Pylera®) or quadruple therapy with levofloxacin and bismuth. In patients receiving triple regimens containing levofloxacin or the standard bismuth quadruple regimen, cure rates were optimized with 14-day regimens using high doses of proton pump inhibitors (PPIs). However, Pylera® or quadruple therapy with levofloxacin and bismuth achieved reliable eradication rates regardless of the PPI dose, duration of therapy, or previous first-line treatment regimen.

Conclusion: Empirical second-line triple therapies generally provided low eradication rates unless they included 14 days of levofloxacin or moxifloxacin. However, high effectiveness was obtained with second-line bismuth-containing quadruple therapies.

Treatment	N	% Use	mITT, N (%)	(95% CI)	PP, N (%)	(95% CI)
Triple-A+L	1,522	33.2	1,341 (81)	(79-83)	1,320 (81)	(79-83)
Pylera (single capsule)	692	15.1	622 (90)	(87-92)	607 (90)	(88-93)
Quadruple-A+L+B	529	11.5	478 (89)	(86-92)	462 (89)	(86-92)
Triple-C+A	477	10.4	231 (81)	(76-86)	226 (81)	(76-86)
Quadruple-M+Tc+B	204	4.4	183 (83)	(77-89)	177 (84)	(78-90)
Quadruple-C+A+M	179	3.9	169 (85)	(79-90)	167 (84)	(79-90)
Triple-A+Mx	143	3.1	135 (91)	(86-96)	135 (91)	(86-96)
Triple-A+M	93	2.0	76 (60.5)	(49-72)	76 (60.5)	(49-72)
Total*	4,862	100%	3,966 (84)	(82-85)	3,966 (84)	(81-83)

[Table 1. Frequency of second-line empirical treatment prescriptions and effectiveness by modified intention-to-treat and per-protocol analyses]

mITT - modified intention-to-treat, PP - per-protocol, 95%CI - 95% confidence interval, C - clarithromycin, M - metronidazole, T - tinidazole, A - amoxicillin, L - levofloxacin, B - bismuth salts, Tc - tetracycline, Mx - moxifloxacin, N - Total of patients receiving an empirical treatment, Total* - accounted also 1,023 (21%) second-line empirical treatments with less than 100 patients treated in each category, that are not reported in the table.

Disclosure: Dr. Nyssen has received research funding from Mayoly, Allergan. Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Mayoly, Allergan, Diasorin.

P0227

BISMUTH QUADRUPLE THREE-IN-ONE SINGLE CAPSULE: 3 OR 4 TIMES DAILY? SUB-ANALYSIS OF THE SPANISH DATA OF THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: Bismuth quadruple with the single capsule Pylera® (PPI, bismuth, tetracycline and metronidazole) includes the intake of 3 capsules four times a day (3c/6h), according to the technical sheet. This scheme may not be suitable for Spanish eating habits; therefore, some physicians prescribe the treatment in the form of 4 capsules three times a day (4c/8h). **Aims & Methods:** To assess the effectiveness and safety of quadruple single capsule bismuth therapy (Pylera®) administered three times a day (4c/8h) in the European Registry on the management of *Helicobacter pylori* (Hp-EuReg).

Methods: Systematic prospective registry of the clinical practice of European gastroenterologists (27 countries) on the management of *H. pylori* infection and its treatment. All infected adult patients were systematically registered at AEG-REDCap e-CRF from June 2013 to June 2019. Extraction and analysis of all cases treated with Pylera® were subject to quality control. Effectiveness was provided for both the modified intention-to-treat and per-protocol sets.

Results: Of the 2,326 Spanish patients treated with Pylera® in the Hp-EuReg, 1,140 (74%) were treated with 3c/6h and 403 (17%) with the 4c/8h scheme. The average age was 48 years, 63% were women, and 11% had a peptic ulcer. Most of the cases (72%) were naïve to treatment. The dose of PPI did not influence eradication rates. Both treatment schedules showed

equivalent compliance, adverse events, and eradication rates (table 1). One patient suffered a serious adverse event (*C. difficile* infection), in the group 3c/6h.

Conclusion: The prescription of quadruple therapy with single capsule bismuth (Pylera®) given as four capsules three times a day seems to have the same compliance, tolerance and effectiveness as the scheme included in the data sheet (three capsules four times a day).

Pylera®	Compliance (%)	AEs (%)	Modified intention-to-treat (%)			Per-protocol (%)		
			Pylera®	Overall	91	Pylera®	Overall	93
4c/8h	97	22	4c/8h	1st line	95	4c/8h	1st line	96
				2nd line	92		2nd line	94
				3rd line	86		3rd line	92
3c/6h	98	24	3c/6h	1st line	93	3c/6h	1st line	95
				2nd line	83		2nd line	87
				3rd line	84		3rd line	86

[Table 1. Effectiveness, compliance and safety of treatment with Pylera® in first-, second-, and third-line.]

AEs: adverse events. 4c/8h: four capsules three times a day (every 8 hours); 3c/6h: three capsules four times a day (every 6 hours).

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P0228

EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): EXPERIENCE WITH SINGLE CAPSULE BISMUTH QUADRUPLE THERAPY IN 3,439 PATIENTS

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Introduction: There has been a resurgence in the use of bismuth-quadruple therapy (PPI, bismuth, tetracycline and metronidazole) in Europe with the commercialization of a single-capsule formulation (Pylera®), but the experience with this regimen is still limited.

Aims & Methods: To evaluate the effectiveness and safety of Pylera® in the European Registry on *Helicobacter pylori* management (Hp-EuReg). International multicenter prospective non-interventional registry aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists. All infected adult patients treated with Pylera® according to data sheet (3 capsules/6h) were systematically registered at AEG-REDCap e-CRF until December 2019. Variables included: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Modified intention-to-treat (mITT) analyses were performed and data were subject to quality review.

Results: Of the 34,460 patients in the Hp-EuReg, 2,100 (6.1%) were prescribed single-capsule bismuth-quadruple therapy (10 days, 3 capsules q.i.d.). The majority of these patients were naïve (63%), with an average age of 50 years, 64% female and 16% with peptic ulcer. Pylera® achieved a high eradication rate based on the mITT (91.9%). Effectiveness was higher when using Pylera® as a first-line treatment (94.6%) but it had also high effectiveness as a rescue therapy, both in second-line (89.3%) or subsequent lines of therapy (3rd-6th line: 91.9%) (Table1). Compliance was the factor most closely associated with the effectiveness of treatment. Adverse events (AEs) were generally mild-to-moderate and transient, only 3% of patients reporting a severe AE, leading to discontinuation of treatment in 1.7% of patients.

Conclusion: The 10-day treatment with single-capsule bismuth-quadruple therapy (Pylera®) achieves *H. pylori* eradication in approximately 90% of patients by mITT in real-world clinical practice, both as a first-line and rescue treatment, with a favourable safety profile.

	Use, N (%)	mITT, N (%)	95% CI	PP, N (%)	95% CI
Overall	2,100 (6*)	1,777 (92)	(91-93)	1,761 (92-94)	(92-94)
Naïve	1,335(63)	1,166 (95)	(93-96)	1,158 (94-97)	(94-97)
2nd line	465 (22)	375 (89)	(86-92)	370 (87-93)	(87-93)
3rd line	212 (10)	174 (89)	(84-93)	177 (83-93)	(83-93)

[Table 1. Pylera® effectiveness (by modified intention-to-treat) in first-, and consecutive rescue treatment lines.]

*Of the total of treatments included in the Hp-EuReg up to December 2019 (i.e. N= 34,460); mITT: modified intention-to-treat; PP: per-protocol, N: total number of patients analysed.

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P0229

SAFETY OF THE TREATMENT OF *H. PYLORI* INFECTION: EXPERIENCE FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG) ON 22,000 PATIENTS

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Introduction: The safety of *Helicobacter pylori* eradication treatments and to what extent adverse events (AEs) may influence therapeutic compliance is unknown.

Aims & Methods: To assess the frequency, type, intensity and duration of AEs, and their impact on compliance, for the most frequently used treatments in the European Registry on *Helicobacter pylori* management (Hp-EuReg). Systematic prospective non-interventional registry of the clinical practice of European gastroenterologists (27 countries, 300 investigators) on the management of *H. pylori* infection in routine clinical practice, promoted by the EHMSG. All prescribed eradication treatments and their corresponding safety profile were recorded in an e-CRF in AEG-REDCap until June 2019. AEs were classified depending on the intensity of symptoms as mild/moderate/severe, and as serious AEs (death, hospitalisation, disability, congenital anomaly and/or requires intervention to prevent permanent damage). All data were subject to quality control.

Results: The different treatments prescribed to a total of 22,492 naïve and non-naïve patients caused at least one AE in 22% of the cases (Table 1), the classic bismuth-based quadruple therapy being the worst tolerated (37% of AEs). Taste disturbance (7%), diarrhoea (7%), nausea (6%) and abdominal pain (3%) were the most frequent AEs. The majority of AEs were mild (57%), 6% were severe, and only 0.08% were serious, with an average duration of 7 days. The treatment compliance rate was 97%. Only 1.3% of the patients discontinued treatment due to AEs.

Conclusion: *H. pylori* eradication treatment frequently induces AEs, although they are usually mild and of limited duration. Its appearance does not interfere significantly with the compliance of treatment.

Adverse events	Yes	%	95%CI
Triple-C+A	1,037	15	(14-16)
Quadruple-C+A+M	926	25	(23-26)
Pylera®	642	28	(26-30)
Quadruple -C+A+B	627	34	(34-37)
Triple-A+L	339	21	(19-23)
Triple-C+M	184	20	(18-23)
Quadruple -A+L+B	180	32	(28-36)
Quadruple -M+Tc+B	84	37	(30-43)
TOTAL	4,298	22	(22-23)

[Table 1. Safety in naïve and non-naïve patients]

CI- confidence interval; A - amoxicillin, C - clarithromycin; M - metronidazole; L - levofloxacin; B; - bismuth; Tc - tetracycline.

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P0230

VONOPRAZAN-AMOXICILLIN DUAL THERAPY FOR *H. PYLORI* INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: *H. pylori* infection is associated with several gastrointestinal and extra-gastrointestinal conditions and is the leading cause of gastric cancer. Its eradication is therefore performed worldwide to improve or prevent these conditions¹. Unfortunately, the eradication rate of the currently available regimens is declining, mostly owing to the increase its resistance to antimicrobials^{1,2}. Several studies have shown the importance of profound and long-lasting acid suppression for *H. pylori* eradication³. Vonoprazan, a novel potassium-competitive acid blocker, provides a stronger and longer-lasting antisecretory effect than proton pump inhibitors. A dual therapy, combining vonoprazan with amoxicillin, could be a simple regimen for *H. pylori* infection and, because it contains a single antibiotic, could allow antimicrobial stewardship compared with triple or quadruple regimens. In addition, since - even after multiple treatments - *H. pylori* resistance to amoxicillin is very low², this dual regimen has the potential to overcome the ever-lower eradication rate of regimens employing clarithromycin, imidazole or/and quinolone antimicrobial agents, toward which resistance is constantly increasing².

Aims & Methods: Performing a systematic review and meta-analysis to evaluate the effectiveness and the safety (adverse events - AEs) of vonoprazan-amoxicillin dual therapy for *H. pylori* eradication. MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials were searched from inception to April 2020. Furthermore, abstract books of major European, American and Asian gastroenterological meetings were also examined. Data for primary and secondary outcomes were pooled using a random effects model.

Results: The search strategy identified 4 studies, all performed in Asia: 2 studies where dual therapy lasted 7 days, and 2 studies where dual therapy lasted 14 days. According to the ITT analysis, the pooled eradication rate was 85.6% (95%CI: 74.8 to 94.0), with evidence of significant

heterogeneity (Cochrane Q: $p = 0.036$; $I^2 = 64.8\%$). According to the PP analysis, the pooled eradication rate was 89.1% (95%CI: 76.9 to 97.5), with evidence of significant heterogeneity (Cochrane Q: $p = 0.008$; $I^2 = 74.7\%$). One study showed an outlier eradication rate, and after its removal, the pooled eradication rate was 88.6% (95%CI: 82.4 to 93.8 - Cochrane Q: $p = 0.264$; $I^2 = 24.9\%$) and 92.8% (95%CI: 85.0 to 98.1 - Cochrane Q: $p = 0.128$; $I^2 = 51.3\%$), according to ITT and PP analysis, respectively. The eradication rate in patients harboring strains resistant to clarithromycin was 95.4% (95% CI: 86.6 to 100). Finally, the overall AEs were 26.5% (95% CI: 20.0 to 33.5), without any severe event.

Conclusion: Vonoprazan-amoxicillin dual therapy provided clinically relevant *H. pylori* eradication rates, even in patients harboring strains resistant to clarithromycin. Further European and North American studies are needed to confirm these results.

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P0231

EMPIRICAL VERSUS SUSCEPTIBILITY-GUIDED TREATMENT OF HELICOBACTER PYLORI INFECTION: A META-ANALYSIS

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Introduction: Treating patients according to antibiotic resistances has frequently been recommended. However, the information on its real effectiveness is scarce.

Aims & Methods: To perform a meta-analysis comparing empirical versus susceptibility-guided treatment of *H. pylori*. *Selection of studies:* comparing empirical versus susceptibility-guided treatment. *Search strategy:* electronic&manual. *Data synthesis:* by intention-to-treat (random effects model).

Results: Overall, 38 studies were included (6,525 patients in the empirical and 5,124 in the susceptibility-guided group). *H. pylori* eradication was achieved in 87% versus 77% respectively (RR:1.13; 95%CI:1.09-1.17; I^2 :77%). Similar results were found when only RCTs were evaluated (22 studies; RR:1.16; 95%CI:1.10-1.22; I^2 :72%). Similar results were also observed when susceptibility testing was assessed by culture (RR:1.13; 95%CI:1.07-1.19) or PCR (RR:1.14; 95%CI:1.05-1.23). When assessing first-line treatments (naïve patients) only (28 studies), better efficacy results were obtained with the susceptibility-guided strategy (RR:1.16; 95%CI:1.11-1.21; I^2 :79%). However, when prescribing empirical first-line quadruple regimens only (both with and without bismuth, excluding the suboptimal triple therapies), no differences in efficacy were found versus the susceptibility-guided group (RR:1.02; 95%CI:0.95-1.09); this lack of difference was confirmed in RCTs not based on CYP2C19 gene polymorphism (RR:1.07; 95%CI:0.98-1.17). For rescue-therapies (13 studies, most as 2nd-

line), similar results were demonstrated with both strategies, both including all studies (RR:1.09; 95%CI:0.97-1.22; I^2 :82%) and also when only RCTs were considered (RR:1.15; 95%CI:0.97-1.36).

Conclusion: The benefit of susceptibility-guided treatment over empirical treatment of *H. pylori* infection could not be demonstrated, either in first-line (if the most updated quadruple regimens are prescribed) or in rescue therapies.

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P0232

EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): CLINICAL PHENOTYPES THROUGH MACHINE LEARNING OF FIRST-LINE TREATED PATIENTS IN SPAIN DURING THE PERIOD 2013-2018

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Introduction: The segmentation of patients in homogeneous groups, according to their clinical variables and treatments, could help to improve the effectiveness of current eradication therapy.

Aims & Methods: 1) To group patients from the European Registry on *Helicobacter pylori* management (Hp-EuReg) according to their demographic and clinical characteristics as well as to the different treatment types by means of a multivariate categorical analysis and, subsequently, a cluster decomposition. 2) To evaluate the treatments' effectiveness in the resulting patients' clusters.

Systematic prospective registry of the routine clinical practice of European gastroenterologists on the management of *H. pylori* infection. First-line empirical treatments were included. The following categorical variables were used: sex, ethnicity, diagnosis, symptoms, therapeutic indication, treatment scheme, duration of treatment, proton-pump inhibitor (PPI) dose, compliance, adverse events, and region of the prescribing center.

Results: In total, 8,322 patients from Spanish centers were analysed from June 2013 to December 2018. Table 1 shows the upward average effectiveness trend of treatments, ranging from 78.4% in 2013 to 92.2% in 2018. The lowest effectiveness, for clusters with more than 100 patients, was obtained in cluster 1 in 2015, with an eradication rate of 82.8%. This cluster was composed by two first-line treatments: triple therapy with PPI-clarithromycin-amoxicillin and concomitant therapy with PPI-clarithromycin-amoxicillin-metronidazole/tinidazole, lasting both 10 days in the vast majority of cases. Pylera® treatment administered together with high PPI doses during 10 days obtained over 95% effectiveness (cluster 3, in 2018), uniformly distributed among Malaga, Valencia, Ciudad Real, Sevilla, Madrid, and Valladolid cities. Concomitant therapy with high PPI dose given for 14 days achieved an effectiveness of 90.7% during the 2018 year (94% of patients in cluster 1), distributed mainly between Malaga, Ciudad Real and Madrid cities.

Conclusion: The cluster analysis allows both identifying homogeneous groups of patients as well as assessing the effectiveness of the different first-line treatments evaluated.

Effectiveness % (number of patients) per cluster						
Year	Number of clusters	1	2	3	4	5
2013	3	89.6 (280)	83.2 (619)	80.0 (80)		
2014	3	88.2 (1685)	69.6 (46)	83.3 (6)		
2015	5	91.6 (83)	89.4 (839)	<u>82.9 (615)</u>	70.8 (24)	88.2 (17)
2016	3	94.7 (359)	86.1 (853)	92.6 (296)		
2017	3	94.3 (630)	90.6 (636)	91.6 (153)		
2018	3	91.8 (122)	90.7 (161)	<u>96.5 (338)</u>		

[Table 1. Trends in the overall effectiveness (by modified intention-to-treat, per cluster) between 2013 and 2018 in Spain]

Simple underlining highlights the lowest effectiveness for groups of more than 100 patients and double underlining the highest effectiveness.

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P0233

REAL-WORLD COMPARATIVE EFFECTS OF THREE-IN-ONE SINGLE CAPSULE BISMUTH QUADRUPLE THERAPY VS. NON-BISMUTH QUADRUPLE CONCOMITANT THERAPY: INTERIM ANALYSIS OF THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: RCTs have strict selection criteria that render results not fully transferable to the clinical practice.

Aims & Methods: To assess the comparative effects of first-line bismuth-single-capsule (PPI-bismuth-tetracycline-metronidazole) vs. non-bismuth quadruple concomitant therapy (PPI-amoxicillin-clarithromycin-nitroimidazole). The European Registry on *H. pylori* management (Hp-EuReg) data from Spain, Italy and Portugal was used to emulate a target trial with prospective observational data, comparing the relative effectiveness (modified intention-to-treat, mITT; and per-protocol, PP) and safety (adverse events, AEs) of first-line bismuth-single-capsule [10 days, 3 PPI dosages] and concomitant therapy [10/14 days; 3 PPI dosages], rendering 9 prescription strategies. Regression analysis controlling for confounders was used to estimate the relative effects of each strategy.

Results: Overall, 2,340 individuals were included. Compared to 10-day concomitant therapy at low PPI doses (n=484), all bismuth-single-capsule combinations presented an eradication incremental benefit by mITT ranging from 7.3% (95%CI:1.1-13%;p=0.024) with low dose PPI to 12.1% (95%CI:5.1-19%;p< 0.001) with standard PPI dose. High PPI dosages in the concomitant therapy resulted in an eradication incremental benefit by mITT ranging from 7.7% (95%CI:2.5-12.8;p=0.003) to 8.8% (95%CI:1.1-16.5;p=0.025) when administered for 14 and 10 days, respectively (table 1). No differences were found with respect to AEs or severe AEs in any of the assessed strategies.

Conclusion: Single-capsule bismuth quadruple therapy and non-bismuth quadruple concomitant therapy appear to have similar risk-benefit ratios when prescribed with high PPI doses.

Strategies	mITT absolute risk difference (95% CI)	P value	PP absolute risk difference (95% CI)	P value
Bismuth-single-capsule, 10 days, low dose PPI	7.4 (1.8-13.1)	0.010	8.9 (3.4-13.5)	0.002
Bismuth-single-capsule, 10 days, standard dose PPI	12.1 (5.1-19.0)	<0.001	12.6 (5.8-9.4)	<0.001
Bismuth-single-capsule, 10 days, high dose PPI	7.3 (0.9-13.6)	0.025	8.3 (2.0-14.5)	0.009
Non-bismuth quadruple concomitant therapy, 10 days, standard dose PPI	8.2 (2.1-14.2)	0.008	8.0 (2.2-13.9)	0.007
Non-bismuth quadruple concomitant therapy, 10 days, high dose PPI	8.8 (1.1-16.5)	0.025	10.0 (2.5-17.6)	0.009
Non-bismuth quadruple concomitant therapy, 14 days, low dose PPI	4.5 (-1.8-10.8)	0.166	4.6 (-1.6-10.8)	0.145
Non-bismuth quadruple concomitant therapy, 14 days, standard dose PPI	7.5 (-0.6-15.5)	0.069	6.8 (-1.0-14.6)	0.088
Non-bismuth quadruple concomitant therapy, 14 days, high dose PPI	7.7 (2.5-12.8)	0.003	7.5 (2.4-12.5)	0.004

[Adjusted estimates* for eradication with respect to non-bismuth quadruple concomitant therapy during 10 days and low dose PPI]

Low dose PPI: ranging from 4.5 to 27 mg omeprazole equivalents, b.i.d. Standard dose PPI: ranging from 32 to 40 mg omeprazole equivalents, b.i.d. High dose PPI: ranging from 54 to 128 mg omeprazole equivalents, b.i.d. Bismuth-single-capsule (PPI-bismuth-tetracycline-metronidazole). Non-bismuth quadruple concomitant therapy (PPI-amoxicillin-clarithromycin-nitroimidazole). *Estimates controlling for: age, sex, ethnicity, indication, concomitant allergy drug, hospital fixed effects and year fixed effects.

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P0234

ANTIBIOTIC RESISTANCE TRENDS OF *HELICOBACTER PYLORI* NAÏVE PATIENTS IN THE PERIOD 2013-2019: ANALYSIS OF THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: Bacterial antibiotic resistance changes over time based on multiple factors. It is essential to study these trends to apply preventive strategies to help reducing such resistances.

Aims & Methods: To conduct a time-trend analysis of the antibiotic resistance to *H. pylori* infection in the European Registry on *H. pylori* (Hp-EuReg). International multicenter prospective non-interventional European Registry on *H. pylori* Management (Hp-EuReg) aiming to evaluate the decisions and outcomes of *H. pylori* infection by European gastroenterologists. All infected adult patients diagnosed with culture and with a result of the antibiotic resistance test were registered at AEG-REDCap e-CRF from 2013 to 2019.

Results: A total of 32,447 patients were included, and culture was performed in 3,474 (11%), where 2,483 naïve patients were included for analysis. Resistance to at least one antibiotic was described in 57% of the patients. Resistance to metronidazole (27%) was most frequent, whereas resistance to tetracycline and amoxicillin was below 1%. Clarithromycin resistance remained above 15% throughout the studied years (Table 1). A significant decrease in the metronidazole resistance rate was observed between 2013 (38%) and 2018 (21%).

Conclusion: In naïve patients, resistance to clarithromycin remained above 15% in the period 2013-2019. A progressive decrease in metronidazole resistance was observed. No increasing or decreasing trend was observed in the bacterial resistance to other antibiotics.

N (%)	2013	2014	2015	2016	2017	2018	2019	Variation range
N° Cultures	435	522	469	286	355	282	310	282-522
No resistance	210 (48)	259 (50)	197 (42)	93 (33)	162 (46)	106 (38)	104 (33.5)	33-50
Clarithromycin (C)	86 (20)	120 (23)	117 (25)	59 (21)	68 (19)	65 (23)	57 (18)	18-25
Metronidazole (M)	165 (38)	156 (30)	140 (30)	72 (25)	64 (18)	60 (21)	66 (21)	18-38
Levofloxacin (L)	58 (13)	100 (19)	103 (22)	46 (16)	59 (17)	55 (20)	41 (13)	13-22
Amoxicillin	6 (1)	0 (0)	0 (0)	0 (0)	10 (3)	1 (0.4)	0 (0)	<1
Tetracyclin	3 (0.7)	1 (0.2)	0 (0)	1 (0.3)	5 (1.4)	0 (0)	1 (0.3)	<1.4
Dual (C+M)	56 (13)	65 (13)	62 (13)	33 (12)	30 (9)	28 (10)	29 (9)	9-13
Triple (C+M+L)	22 (5)	31 (6)	32 (7)	16 (6)	12 (3)	12 (4)	8 (3)	3-7

[Table 1. Antibiotic resistance trends (2013-2019) of *Helicobacter pylori* naïve patients in Europe. C: clarithromycin; M: metronidazole; L: lefloxacin]

C: clarithromycin; M: metronidazole; L: lefloxacin

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P0235

THE LONG-TERM EFFECT OF THE ERADICATION OF *HELICOBACTER PYLORI* IN T2DM OR PREDM PATIENTS

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Introduction: The positive relationship between *Helicobacter pylori* (H. pylori) infection and extra-gastrointestinal disease has been revealed in several studies. However, the long-term effect of H. pylori eradication on the metabolic syndrome or diabetes mellitus (DM) have not been established, yet.

Aims & Methods: The aim of this study was to evaluate the effect of H. pylori eradication on glycemic control in type 2 DM (T2DM) or preDM patients. From Dec 2006 to Feb. 2019, 3,608 subjects were enrolled at Seoul National University Bundang Hospital who received esophagogastroduodenoscopy. 147 subjects with T2DM or preDM were selected and were divided in three groups, H. pylori-negative (n=40), H. pylori-positive with non-eradicated (n=57) and eradicated group (n=50). H. pylori was diagnosed by culture, histology, CLOtest and Anti-H. pylori IgG antibodies. HbA1c was measured before an eradication therapy or an enroll date in case of H. pylori-negative and non-eradicated group. The follow-up points were 1 year and 5 years after enrollment. For the statistical significance of HbA1c changes according to follow up period in three groups, a linear mixed model was used. P-value < 0.05 was regarded as statistically significant.

Results: There were no significant baseline differences of HbA1c among H. pylori-negative, H. pylori-positive with non-eradicated and eradicated group. In H. pylori-eradicated group, the values of HbA1c were significantly decreased after the eradication compared to H. pylori-negative and H. pylori-positive with non-eradicated groups in each 1 and 5 year points. In subgroup analysis, HbA1c values decreased in the patients who are male and/or age under 65 in the eradicated group compared to other groups. In contrast, HbA1c changes were not different among three groups in female or aged group over 65. We also proved the interaction between follow up period and group difference adjusted for age, sex, smoke, alcohol (Table 1). The eradication of H. pylori had significant effect on improvement of HbA1c values through follow up period compared to non-eradicated group at 1 and 5 year follow-up. However, TG and HDL has no statistically significant difference between three groups.

	Estimate	P value
Age<65 vs ≥ 65	0.34 (0.15)	0.021
Male vs female	0.05 (0.22)	0.811
Non vs Current/ex-smoker	0.06 (0.22)	0.782
Non vs Current/ex-drinker	-0.25 (0.16)	0.130
H. pylori negative * 1 year‡	0.04 (0.14)	0.778
Eradicated * 1 year‡	-0.31 (0.13)	0.016
H. pylori negative * 5 year‡	-0.06 (0.16)	0.735
Eradicated * 5 year‡	-0.48 (0.15)	0.001

Data are presented as mean (standard error). Adjusted variables: age, sex, smoke, alcohol. ‡: The interaction between H. pylori status and follow up period (1 and 5 years). P value : adjusted P value; compared to Non-eradicated group.

[Multivariate analysis regarding changes in HbA1c according to H. pylori status]

Conclusion: H. pylori eradication decreased HbA1c level in T2DM or DM patients for long term follow up period, especially in male subjects and age under 65, which support the rationale for recommendation of H. pylori eradication therapy in male or young patients with T2DM or preDM.

Disclosure: Nothing to disclose

P0236

ROOM FOR IMPROVEMENT IN THE TREATMENT OF *HELICOBACTER PYLORI* INFECTION: LESSONS FROM THE EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG)

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Introduction: Managing *Helicobacter pylori* infection requires constant decision-making, and each decision is open to possible errors.

Aims & Methods: To evaluate common mistakes in the eradication of H. pylori, based on the European Registry on *Helicobacter pylori* management (Hp-EuReg). Hp-EuReg is an international multicentre prospective non-interventional registry evaluating the decisions and outcomes of H. pylori management by European gastroenterologists in routine clinical practice.

Results: Countries recruiting more than 1,000 patients were included (26,340 patients). The most common mistakes (percentages) were: 1) To use the standard triple therapy where it is ineffective (46%). 2) To prescribe eradication therapy for only 7-10 days (69%) (Table 1). 3) To use a low dose of proton pump inhibitors (48%). 4) In patients allergic to penicillin, to prescribe always a triple therapy with clarithromycin and metronidazole (38%). 5) To repeat certain antibiotics after eradication failure (>15%). 6) To ignore the importance of compliance with treatment (2%). 7) Not to check the eradication success (6%). Time-trend analyses showed progressive greater compliance with current clinical guidelines.

Conclusion: The management of *H. pylori* infection by European gastroenterologists is heterogeneous, frequently suboptimal and discrepant with current recommendations. Clinical practice is constantly adapting to updated recommendations, although this shift is delayed and slow.

	7 or 10 days		14 days		
	Mistake (%) ¹	mITT (%)	14-days use, N (%)	mITT, N (%)	95%CI
Spain	71	71	1,429 (29)	1,297 (86)	(83-87)
Russia	63	77	984 (37)	790 (90)	(88-92)
Slovenia	62	85	1,070 (38)	722 (91)	(89-93)
Italy	93	84	28 (7)	21 (67)	(43-85)
Lithuania	84	75	182 (16)	1 (100)	(1.3-99)
Total	69	81	3,693 (31)	2,831 (88)	(87-89)

[Table 1. Use and effectiveness of 7, 10 and 14-day triple regimens in Europe.]

N: total number of patients, mITT: modified intention-to-treat, PP: per-protocol, CI: confidence interval, ¹% of mistake accounted for 7 or 10 day-treatment durations.

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P0237 WITHDRAWN

P0238
BISMUTH QUADRUPLE REGIMEN WITH TETRACYCLINE OR DOXYCYCLINE VERSUS PYLERA® AS THIRD-LINE RESCUE THERAPY FOR *H. PYLORI* INFECTION: A PROSPECTIVE MULTICENTER ANALYSIS OF THE EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: Different bismuth-quadruple therapies containing proton pump inhibitors, bismuth, metronidazole, and a tetracycline have been recommended as third-line *Helicobacter pylori* eradication treatment after failure with clarithromycin and levofloxacin.

Aims & Methods: To evaluate the efficacy and safety of third-line treatments with bismuth, metronidazole and either tetracycline or doxycycline. Sub-study of the European Registry on *H. pylori* Management (Hp-EuReg), an international multicenter prospective non-interventional registry of the routine clinical practice of European gastroenterologists. After previous failure with clarithromycin- and levofloxacin-containing therapies, patients receiving a third-line regimen with 10/14-day of PPI, bismuth, metronidazole and either tetracycline (T) or doxycycline (D), or 10-day Pylera® (P). Data were registered at AEG-REDCap online database.

Results: Four-hundred and fifty-four patients have been treated so far: 85 with T, 94 with D, and 275 with P. Average age was 53 years, 68% were women. Overall modified intention-to-treat and per-protocol eradication rates were 81% (D: 65%, T: 76%, P: 88%) and 82% (D: 66%, T: 77%, P: 88%), respectively. Further details on the effectiveness and compliance of each treatment group according to the length are presented in Table 1. By logistic regression, higher eradication rates were associated with compliance (OR=2.96; 95%CI=1.01-8.84) and no prior metronidazole use (OR=1.96; 95%CI=1.15-3.33); P was superior to D (OR=4.46; 95%CI=2.51-8.27), and T marginally superior to D (OR= 1.67; 95%CI=0.85-3.29).

Conclusion: Third-line (after failure with clarithromycin and levofloxacin) *H. pylori* eradication with bismuth quadruple treatment offers acceptable efficacy and safety. Highest efficacy was found in compliant patients and in those taking 10-day Pylera® or 14-day tetracycline. Doxycycline seems to be less effective and therefore should not be recommended.

Effectiveness, N (%)		Compliance	mITT, N	mITT (95%CI)	PP, N	PP (95%CI)
Group T	Overall	82 (97%)	64	76% (66-86)	63	77% (67-86)
	10 days*	29 (97%)	19	66% (47-85)	19	66% (47-85)
	14 days	45 (96%)	45	82% (71-93)	44	83% (72-94)
Group D	Overall	85 (93%)	58	65% (55-76)	56	66% (55-77)
	10 days*	37 (90%)	25	63% (46-79)	23	63% (45-79)
	14 days	53 (96%)	32	70% (55-84)	32	71% (57-85)
Group P	10 days*	249 (96%)	222	88% (83-92)	216	88% (84-92)

[Table 1. Effectiveness (by modified intention-to-treat and per-protocol) and compliance according to the treatment regimen and length]

Group T - tetracycline containing bismuth quadruple therapy, Group D - doxycycline containing bismuth quadruple therapy, Group P - single capsule bismuth quadruple therapy (Pylera®), 95%CI - 95% confidence interval. ITT: intention-to-treat, mITT: modified intention-to-treat; PP: per-protocol. The Chi² test showed statistically significant differences of treatment length in the mITT set between treatment groups (T, D and P) as reported in the table: *p < 0.001.

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P0239

IMPACT OF *HELICOBACTER PYLORI* CLARITHROMYCIN RESISTANCE ON THE TREATMENT EFFECTIVENESS: DATA OF THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: Antibiotic resistance is the major factor affecting our ability to cure *Helicobacter pylori* infection. Quadruple therapy is currently recommended; however, triple therapy with two antibiotics may be sufficient in those patients without clarithromycin resistance.

Aims & Methods: To evaluate the effectiveness of the treatments according to the clarithromycin *H. pylori* resistance in Europe. International multicenter prospective non-interventional European Registry on *H. pylori* Management (Hp-EuReg) aiming to evaluate the decisions and outcomes of *H. pylori* infection. Infected adult patients diagnosed with culture registered at AEG-REDCap e-CRF from 2013 to 2019. Per-protocol (PP) analysis was performed based on the presence or absence of clarithromycin bacterial resistance.

Results: Overall, 5,036 patients were included: 1,747 (35%) were resistant and 3,289 (65%) sensitive to clarithromycin. The overall eradication rate was higher in clarithromycin-susceptible patients (91% vs. 84%; $p < 0.001$). Triple therapy with a PPI, clarithromycin and amoxicillin achieved over 90% eradication rates in clarithromycin-susceptible patients. However, in those with clarithromycin-resistance, optimal effectiveness was only achieved when treated with quadruple therapy with a PPI, clarithromycin, amoxicillin and bismuth (Table 1).

Conclusion: Classic triple therapy with a PPI, clarithromycin and amoxicillin achieves optimal results (>90%) in patients susceptible to clarithromycin. However, when clarithromycin resistance is unknown, quadruple therapy with a PPI, clarithromycin, amoxicillin and bismuth may be a better treatment option.

Treatment schemes	Clarithromycin resistant (E/N,%)			Clarithromycin susceptible (E/N,%)		
Triple-C+A	11	14	79%	392	431	91%
Triple-A+L	165	191	86%	47	55	85%
Triple-A+M	46	55	84%	147	166	89%
Triple-A+R	91	102	89%	9	11	82%
Quadruple-C+A+M/T	43	54	80%	88	100	88%
Quadruple-C+A+B	10	11	91%	36	40	90%
Sequential-C+A+T	242	286	85%	627	664	94%
Sequential-C+A+M	17	23	74%	41	53	77%
Single capsule	66	80	83%	53	54	98%

[Table 1. Effect of the clarithromycin *Helicobacter pylori* resistance on the effectiveness of treatments in Europe]

E: number of eradicated patients N: total number of patients analysed; %: per-protocol effectiveness; C: clarithromycin; M: metronidazole; B: bismuth; A: amoxicillin; T: tinidazole; Single capsule: three-in-one single capsule containing bismuth, tetracycline and metronidazole (marketed as Pylera®)

Disclosure: Dr Luis Bujanda has no conflicts of interest to declare. Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Mayoly, Allergan, Diasorin.

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HELICOBACTER PYLORI ANTIBIOTIC RESISTANCE: DATA FROM THE EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG)

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Introduction: Antibiotic resistance is the major factor affecting our ability to cure *Helicobacter pylori* infection. Understanding the different *H. pylori* antibiotic resistances could be the key to improve treatment effectiveness.

Aims & Methods: To evaluate the *H. pylori* antibiotic resistance both prior and after one or several eradication treatments, in order to provide the most appropriate recommendations for the eradication of *H. pylori*.

International multicenter prospective non-interventional European Registry on *H. pylori* Management (Hp-EuReg) aiming to evaluate the decisions and outcomes of *H. pylori* infection by European gastroenterologists. Infected adult patients diagnosed with culture and with a result of the antibiotic resistance test registered at AEG-REDCap e-CRF from 2013 to 2019. Per-protocol (PP) analysis was performed. The antibiotic bacterial resistances were described by treatment line.

Results: A total of 32,447 patients were included, and culture was performed in 3,474 (11%). In naïve patients, 21% reported single clarithromycin resistance, and 11% dual (clarithromycin and metronidazole) resistance. Antibiotic resistance increased markedly from the first treatment, reaching over 37% dual resistance in second-line treatment (Table 1).

Conclusion: In Europe, culture testing to determine antibiotic resistance against *H. pylori* is scarce. *H. pylori* single clarithromycin resistance remains high (>15%) in all treatment lines, and greater than 20% in naïve patients. Dual or triple resistances are frequent and increase remarkably after the first treatment failure. Resistance to amoxicillin or tetracycline is exceptional.

Treatment line	Naïve (%)	Second (%)	Third (%)	Fourth (%)	Fifth (%)	Sixth (%)	p-value
Number of patients	2,485	521	311	97	31	11	
No resistance	1,054 (42)	74 (14)	26 (8)	7 (7)	4 (13)	1 (9)	< 0.001
Clarithromycin (C)	531 (21)	298 (57)	217 (70)	72 (74)	23 (74)	5 (45)	< 0.001
Metronidazole (M)	674 (27)	251 (48)	192 (62)	59 (61)	19 (61)	7 (64)	< 0.001
Levofloxacin (L)	438 (18)	134 (26)	130 (42)	44 (45)	12 (39)	3 (27)	< 0.001
Amoxicillin	17 (1)	4 (1)	5 (2)	0 (0)	0 (0)	0 (0)	< 0.001
Tetracycline	11 (0.4)	3 (1)	2 (0.6)	1 (1)	0 (0)	0 (0)	> 0.05
Dual (C+M)	279 (11)	195 (37)	165 (53)	52 (54)	17 (55)	5 (46)	< 0.001
Triple (C+M+L)	128 (5)	91 (18)	99 (32)	34 (35)	9 (29)	3 (27)	< 0.001

[Table 1. *Helicobacter pylori* antibiotic resistances (by treatment line) in Europe]

C: clarithromycin; M: metronidazole; L: levofloxacin

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P0241 WITHDRAWN

P0242

EFFECTIVENESS OF FIRST-LINE *H. PYLORI* ERADICATION THERAPY ACCORDING TO THE DAILY STATIN-USE: ANALYSIS OF THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: The use of statins combined with antibiotics has been suggested as a strategy to increase the effectiveness of *Helicobacter pylori* treatments, mainly based on their anti-inflammatory characteristics. However, evidence published so far still remains scarce.

Aims & Methods: Aim: To analyse the impact of the daily use of statins in the effectiveness of *H. pylori* first-line therapies in a European cohort of patients.

Methods: Multicentre prospective non-interventional study of the clinical practice of European gastroenterologists of the European Registry on *H. pylori* Management (Hp-EuReg). Patients were collected at AEG-REDCap e-CRF from 2013 to December 2019. Records of naïve patients containing information about the statins' use were collected and only those daily statin users were considered for current analysis. Modified intention-to-treat (mITT) analysis was performed to evaluate the treatment effectiveness between statin and non-statin users. A multivariate analysis was performed on the overall population and for each treatment scheme, where the dependent variable was the eradication rate by mITT. The independent factors evaluated were: age, gender, presence of ulcer, proton pump inhibitor dose, therapy duration, compliance and use of statins.

Results: Overall, 7,687 patients received an empirical first-line therapy. Median age was 56 years, 60% were women and 18% had peptic ulcer disease. From those, 1,895 (25%) were daily statins-users: 45% used simvastatin, 35% atorvastatin, 11% rosuvastatin and 9% other statins. Univariate analysis showed no differences in the treatment effectiveness of the statin-users group versus no statin-users on the overall population, neither by therapy prescribed (Table). Concerning the multivariate analysis, the daily statin-use in those patients receiving a standard triple therapy with clarithromycin and amoxicillin was associated with lower treatment effectiveness (OR=0.8; 95%CI: 0.6-0.99). This negative association was not confirmed when the overall population was analysed.

Conclusion: The daily use of statins does not seem to increase the effectiveness of *H. pylori* eradication treatment.

	Daily use of statins	mITT, N (%)	Differences (p-value)
Overall	No	4,835 (88)	p=0.44
	Yes	1,729 (88.5)	
PPI + C + A	No	1,790 (86)	p=0.05
	Yes	544 (82)	
PPI + C + M	No	380 (82)	p=0.52
	Yes	95 (79)	
PPI + Bi + Tc + M	No	616 (94.5)	p=0.69
	Yes	287 (95)	
PPI + C + A + M (Sequential)	No	53 (81)	p=0.32
	Yes	27 (93)	
PPI + C + A + M (Concomitant)	No	1,189 (88)	p=0.08
	Yes	527 (91)	
PPI + Bi + C + A	No	612 (88)	p=0.12
	Yes	186 (92.5)	

[Table 1: Impact of the statins' use on the effectiveness of most frequently used first-line empirical treatments in Europe.]

mITT: modified intention-to-treat. N: number of patients included.
 %: proportion of patients showing effectiveness. PPI: proton pump inhibitor. C: clarithromycin. A: amoxicillin. M: metronidazole. Bi: bismuth. Tc: tetracycline. Sequential: sequential administration of the treatment components. Concomitant: concomitant administration of the treatment components
Disclosure: Dr. M. Caldas has nothing to disclose. Dr. J.P. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Mayoly, Allergan, Diasorin.

P0243 EFFECTIVENESS OF FIRST-LINE *HELICOBACTER PYLORI* ERADICATION TREATMENTS IN SPAIN: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: In Spain, the prescription of *Helicobacter pylori* treatment is mainly empirical, based on previous local effectiveness rates reported in this area. Updated data from routine clinical practice represent a useful source of information contributing to implement treatment strategies.
Aims & Methods: To analyse the effectiveness of *H. pylori* first-line eradication therapies in a Spanish cohort.
 Systematic multicentre prospective registry of the clinical practice of gastroenterologists on the Management of *H. pylori* infection (Hp-EuReg). All infected adult patients were registered at AEG-REDCap e-CRF from Feb-

ruary 2013 to June 2019. Data were subject to quality control. Effectiveness (by modified intention-to-treat, mITT) and multivariate analysis were performed. Independent factors evaluated were: age, gender, presence of ulcer, proton pump inhibitor (PPI) dose, therapy duration and compliance. **Results:** Overall, 10,267 naïve patients receiving an empirical treatment prescription and recruited among 53 Spanish hospitals were included. Median age was 50 years, 61% were women and 15% had peptic ulcer disease. The empirical therapies most frequently prescribed were (all of them including a PPI): the non-bismuth quadruple concomitant therapy (40%), the standard triple therapy containing clarithromycin and amoxicillin (26%), the bismuth three-in-one single capsule containing metronidazole, bismuth and tetracycline (16%), and the bismuth-clarithromycin-amoxicillin quadruple therapy (10%). Other therapies were given in 8% of the cases. Over 90% mITT eradication rate was obtained with 14-day quadruple therapies or with the 10-day bismuth single capsule (Table). Adverse events occurred in 25% of the cases, 0.2% of them being serious. Multivariate analysis reported that being compliant (>90% drug intake; OR=4.1; 95%CI: 3.0-5.5), longer duration therapies [10 days (OR=4.5; 95%CI: 3.2-6.2) or 14 days length (OR=4.1; 95%CI: 2.9-5.9)], higher acid gastric inhibition [standard PPI doses (OR=1.4; 95%CI: 1.2-1.7) or high PPI doses (OR=2.1; 95%CI: 1.7-2.4)] and the presence of ulcer (OR=1.2; 95%CI: 1.0-1.5), were associated with higher mITT eradication rates.

Conclusion: In Spain, optimal effectiveness (>90%) in first-line treatment was obtained with the non-bismuth concomitant therapy, the bismuth-clarithromycin-amoxicillin quadruple therapy (both for 14 days) and the 10-day bismuth single capsule therapy.

	Length (days)	Eradication rate				Safety	
		mITT, N (%)	95% CI	PP, N (%)	95% CI	AE, N (%)	95% CI
Overall	7	159 (60)	52-68	158 (61)	53-68	159 (3.1)	1-7
	10	6,011 (88)	87-89	5,858 (89)	88-90	6,167 (22)	21-23
	14	3,522 (90)	89-91	3,449 (90)	89-91	3,574 (33)	31-34
PPI + C + A + M (Conc)	10	2,232 (88)	87-90	2,175 (89)	88-90	2,296 (26)	24-28
	14	1,629 (92)	91-93	1,588 (92)	91-94	1,648 (30)	28-32
PPI + C + A	7	146 (59)	51-67	145 (59)	51-67	146 (2.7)	1-7
	10	1,686 (84)	82-86	1,657 (84.5)	83-86	1,737 (10)	9-12
	14	699 (86)	84-89	683 (87)	84-89	719 (28)	25-31
PPI + single capsule	10	1,533 (95)	94-96	1,507 (96)	95-97	1,558 (25)	23-27
PPI + Bi + C + A	14	1,004 (91)	89-93	992 (91)	89-93	1,008 (41)	38-44

[Table 1: Effectiveness and safety of the most-frequently prescribed first-line therapies in Spain.]

mITT: modified intention-to-treat. N: number of patients analysed. %: proportion of patients showing the event (effectiveness or the adverse event). CI: confidence interval. PP: per protocol. AE: adverse events. PPI: proton pump inhibitor. C: clarithromycin. A: amoxicillin. M: metronidazole. Single capsule: three-in-one single capsule containing bismuth, tetracycline and metronidazole. Bi: bismuth. Conc: concomitant administration of the drugs.

Disclosure: Dr. M. Caldas has nothing to disclose. Dr. J.P. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Mayoly, Allergan, Diasorin.

P0244 WITHDRAWN

P0245

HOW TO ENHANCE A RESISTANCE OF GASTRIC MUCOSAL BARRIER IN PATIENTS WITH HELICOBACTER PYLORI ASSOCIATED CHRONIC GASTRITIS AND CONCOMITANT TYPE 2 DIABETES MELLITUS?

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Introduction: Patients with type 2 diabetes mellitus (T2DM) are thought to have specific pathogenetic pathways in gastrointestinal (GI) diseases onset. Complications of T2DM may affect GI tract leading to structural and functional changes in organs. The importance of connection between stomach function and T2DM is obvious: normal state of GI system provides better control of glycemia, and maintenance of glycemia within normal limits prevents further complications, including those that have an influence on GI tract. The role and peculiarities of *Helicobacter pylori* (HP) infection in patients with T2DM are still controversial and need more studies to be conducted. Thus, an investigation of pathogenesis of gastric pathology in case of HP infection and its therapeutic correction in patients with T2DM is relevant nowadays.

Aims & Methods: The aim: To study the state of gastric mucosal barrier in patients with HP-positive chronic gastritis (CG) and concomitant T2DM in comparison to non-diabetic subjects. To investigate if the treatment with Eupatilin enhances a resistance of gastric mucosal barrier in patients undergoing triple antihelicobacter therapy (AHT) with Amoxicillin 1000 mg bid, Clarithromycin 500 mg bid and Pantoprazole 40 mg bid for 14 days. **Methods:** A total of 80 patients with endoscopically and histologically confirmed HP-positive (assessed with HP antigen stool test) chronic gastritis were randomly selected to make 2 equal in number groups: I (n=40) - those who had HP-positive CG and concomitant T2DM; II (n=40) - patients with HP-positive CG without T2DM. All patients with T2DM had no signs of diabetes decompensation and the level of HbA1c was less than 7.5%. Patients were further subdivided into 2 groups according to the prescribed treatment: patients of groups Ia (n=20) and IIa (n=20) underwent standard triple AHT; groups Ib (n=20) and IIb (n=20) - standard triple AHT and eupatilin 60 mg tid for 28 days.

Levels of fucose and N-acetylneuraminic acid (NANA) were investigated in blood serum before and after the treatment on the 28th day.

Results: Mean age in the group I was 59.2±7.4 years and in the group II – 41.6±6.2 years, distribution of male/female was 23/17 in the group I, and 21/19 – in the group II. The levels of NANA in patients of the groups I and II before the treatment were 7.87±0.9 mmol/L and 6.78±1.0 mmol/L, while levels of fucose were 2.48±0.76 mmol/L and 1.70±0.42 mmol/L respectively. Thus, patients with T2DM have initially significantly higher levels of NANA and fucose in case of HP-positive chronic gastritis (p<0.05).

AHT reduces NANA and fucose levels statistically significantly in all subgroups (p<0.05). In the group Ia NANA decreased 1.4 less, in Ib – 2.0 times less, IIa – 1.4 times less and in IIb – 2.2 times less in comparison to data before the treatment. Fucose levels decreased 1.7 times less in group Ia, 1.8 times less in group Ib, 1.1 times less in group IIa, 1.4 times less in group IIb. In patients with CG and T2DM Eupatilin prescription in addition to AHT allows to reduce level of NANA 1.5 times less (p<0.05) and level of fucose 1.1 times less than AHT itself.

Conclusion: Mucosal barrier resistance in HP-associated CG is weaker in patients with T2DM than in individuals without DM. AHT targets HP eradication, which also helps to normalize stomach mucus production. Eupatilin addition to triple AHT may potentiate this effect, probably, through its cytoprotective action.

Disclosure: Nothing to disclose

P0246

EFFECTIVENESS OF SECOND-LINE *HELICOBACTER PYLORI* ERADICATION TREATMENTS IN SPAIN: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: Optimal second-line regimens to treat *Helicobacter pylori* infection should be based on local previous results. This strategy is required in order to reach the highest effectiveness by reducing the necessity of further treatment lines, specially considering the increasing rates of multi-resistant bacterial strains worldwide.

Aims & Methods: To analyse the effectiveness of *H. pylori* second-line eradication therapies in a Spanish cohort.

Systematic multicentre prospective registry of clinical practice of gastroenterologists on the management of *H. pylori* infection (Hp-EuReg). All infected adult patients were registered at AEG-REDCap e-CRF from February 2013 to June 2019. Data were subject to quality control. Effectiveness (by modified intention-to-treat, mITT) and multivariate analysis were performed. Independent factors evaluated were: age, gender, presence of ulcer, proton pump inhibitor (PPI) dose, therapy duration, use of clarithromycin in the previous line, and compliance.

Results: Overall, 2,448 patients receiving an empirical second-line treatment and recruited among 53 Spanish hospitals, were included. Median age was 50 years, 66% were women and 94% of the patients had received clarithromycin in the first-line treatment attempt. The therapies more frequently prescribed were (all of them including a PPI): the triple levofloxacin-amoxicillin therapy (39%), the quadruple amoxicillin-levofloxacin-bismuth therapy (19%), the quadruple bismuth three-in-one single capsule containing metronidazole, bismuth and tetracycline (19%) and the triple moxifloxacin-amoxicillin therapy (6%). Other therapies were given in 17% of the cases. Nearly 90% mITT eradication rate was obtained with either moxifloxacin or levofloxacin containing triple therapies, with the quadruple bismuth-levofloxacin therapy (all given for 14 days) or with the 10-day bismuth single capsule therapy (Table). Only 1 patient (0.2%) reported a serious adverse event. Multivariate analysis showed that compliance (>90% drug intake; OR=3.4; 95%CI: 1.7-6.9), high PPI dose (OR=1.9; 95%CI: 1.4-2.6) and 14-day therapy (OR=1.5; 95%CI: 1.1-2.1) were significantly associated with higher mITT eradication rates.

Conclusion: In Spain, optimal effectiveness (approximately 90%) in second-line treatment was obtained with triple quinolone or quadruple bismuth-quinolone regimens (both for 14 days) or with the 10-day bismuth single capsule therapy.

		Eradication rate				Safety	
		Length (days)	mITT, N (%)	95% CI	PP, N (%)	95% CI	AE, N (%)
Overall	10-14	1,265 (79) 1,007 (89)	77-81 87-91	1,241 (80) 986 (90)	77-82 88-92	1,303 (18) 1,020 (42)	16-20 39-45
PPI + L + A	10-14	647 (74) 241 (92)	70-77 88-95	636 (74) 240 (92.5)	70-77 88-96	668 (11) 246 (65)	9-14 59-71
PPI + Bi + L + A	14	444 (90)	86-92	428 (90)	87-93	448 (33)	28-37
PPI + single capsule	10	399 (88.5)	85-91	390 (89)	86-92	411 (30)	26-35
PPI + Mx + A	10-14	20 (100) 109 (89)	NA 82-94	20 (100) 109 (89)	NA 82-94	21 (5) 112 (21)	0-24 14-30

[Table 1: Effectiveness and safety of the most frequently prescribed second-line therapies in Spain.]

mITT: modified intention-to-treat. PP: per-protocol. N: number of patients analysed. %: proportion of patients showing the event (effectiveness or the adverse event). CI: confidence interval. AE: adverse event. PPI: proton pump inhibitor. L: levofloxacin. A: amoxicillin. Bi: bismuth. Single capsule: three-in-one single capsule containing bismuth, tetracycline and metronidazole. Mx: moxifloxacin. NA: non-applicable.

Disclosure: Dr. M. Caldas has nothing to disclose. Dr. J.P. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Mayoly, Allergan, Diasorin.

P0247

IMPACT OF HELICOBACTER PYLORI INFECTION ON COLORECTAL CANCER AND ADENOMA FREQUENCY

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Introduction: *Helicobacter pylori* infection (*Hp-I*) has been recognized as a substantial risk agent involved in gastrointestinal (GI) tract tumorigenesis by stimulating cancer stem cells (CSCs), oncogenes, immune surveillance processes and triggering GI microbiota dysbiosis.

Aims & Methods: The aim of this study was to investigate the possible involvement of active *Hp-I* in the sequence: chronic inflammation-adenoma-colorectal cancer (CRC) development.

Four pillars were investigated: a. endoscopic and conventional histological examinations of patients with CRC, colorectal adenomas (CRA) versus controls to detect the presence of active *Hp-I*; b. immunohistochemical determination of presence of *Hp*; expression of CD44, an indicator of CSCs and/or bone marrow-derived stem cells (BMDSCs); expressions of onco-gene Ki67 and anti-apoptotic Bcl-2 protein; c. expression of CD45, indicator of immune surveillance locally (assessing mainly T and B lymphocytes locally); and d. correlation of the studied parameters with the presence or absence of *Hp-I*.

Results: Among 50 patients with CRC, 25 with CRA and 10 controls, a significantly higher presence of *Hp-I* in the CRA (68%) and CRC group (84%) were found compared with controls (30%). Presence of *Hp-I* with accompanying immunohistochemical expression of CD44 in biopsy specimens was revealed in a high proportion of patients with CRA associated with moderate/severe dysplasia (88%) and CRC patients with moderate/severe degree of malignancy (91%). Comparable results were also obtained for Ki67, Bcl-2 and CD45 immunohistochemical expressions.

Conclusion: *Hp-I* seems to be involved in the sequence: CRA - dysplasia - CRC, similarly to the upper GI tract oncogenesis, by several pathways.

Beyond *Hp-I* associated insulin resistance, the major underlying mechanism responsible for the metabolic syndrome (MetS) that increase the risk of colorectal neoplasms, as implied by other *Hp-I* related MetS pathologies, such as non-alcoholic fatty liver disease and upper GI cancer, the disturbance of the normal GI microbiota (i.e., dysbiosis) and the formation of an irritative biofilm could contribute to a perpetual inflammatory upper GIT and colon mucosal damage, stimulating CSCs or recruiting BMDSCs and affecting oncogenes and immune surveillance processes. Further large-scale relative studies, with pathophysiological perspective are necessary to demonstrate this relationship.

Disclosure: Nothing to disclose

Poster presentations

Small intestinal

Poster Presentations Small intestinal

Small intestinal

09:00-19:00 / Poster Exhibition

P0248 WITHDRAWN

P0249

EFFECTS OF HEALING EARTH IN VITRO AND IN VIVO WITH REGARD TO HISTAMINE (H) BINDING AND REDUCTION OF H-MEDIATED SYMPTOMS - A PROMISING APPROACH FOR H INTOLERANCE SYNDROME (HIS) AND IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: In allergy, IBS, mast cell activation and food intolerance, the absorption of biogenic amines by the intestine as well as H release by mast cells play an important role. These patients often report H-mediated symptoms, are treated by avoiding certain foods or by giving antihistamines. Naturally pure healing earth from glacial loess, a composition of minerals and trace elements, has a large surface area, detoxifies radicals and has the potential to bind various substances such biogenic amines.

Aims & Methods: In vitro approach, it was first examined whether and to what extent healing earth can bind H. Physical binding studies with 10 or 40 mg H on 20 g LUVOS healing earth were carried out for 1 and 2 h at 37 °. The amount of H at time 0 or after 1 and 2 h was determined using the HPLC / DAD method.

In a non-interventional study over 20 days, 27 pts. with known HIS ingested 3 x 6.5 g healing earth/die. A subjective scoring system, tolerance, side effects and pain score were recorded in order to determine a possible effectiveness of the healing earth through the binding of H.

Results: Compared with controls (100% H recovery), 20 g healing earth could achieve a binding of approx. 35% or 48% of the H used < 60 min. with the 10 or 40 mg H dose in vitro [Δ reduction 0.73- or 3.75mg/dl]. Further binding by longer incubation showed no additional effect.

Interestingly, Five pts. (18.5%) completely lost their symptoms and showed complete remission; four of them were able to do without the H-free diet.

7/27 pts. (25.9%) showed a very clear regression of their H symptoms (>75%) compared to the score before therapy, 8 (29.6%) a good symptom reduction (50-75%). The remaining 7 pts. (26%) were unchanged by healing earth.

Conclusion: Healing earth provided by Luvos showed a potentially therapeutic binding effect for H in vitro. As H concentrations are much lower in vivo, it is concluded that healing earth is responsible for luminal H binding in the patients. This effect was found beneficial to reduce H symptoms in more than two thirds of the pts. In view of increasing numbers of allergy, HIS and mast cell-related diseases, healing earth can represent a potentially significant, non-immunosuppressive alternative therapeutic target for controlled prospective studies in this field.

Disclosure: Nothing to disclose

P0250

MEAN PLATELET VOLUME (MPV): IS IT A USEFUL MARKER IN CROHN'S DISEASE PATIENTS?

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Introduction: Many non invasive tests have been studied for diagnosis and determining the activity degree of Crohn's disease (CD) such as the erythrocyte sedimentation rate (ESR) and the c-reactive protein (CRP). Nevertheless, an ideal test has not been found yet. The mean platelet volume (MPV) is provided by automatic hemogram determination devices and it is influenced by inflammation.

Aims & Methods: The aim of this study was to investigate whether the MPV would be useful in CD's activity.

This was a comparative retrospective study of 122 cases of CD (66 men and 56 women, a sex ratio of 1.17) with an average age of 39 years (18-93 years).

As a control group, we used 70 patients consulting for Helicobacter Pylori (HP) gastritis (43 women and 37 men) whose average age was 42 years. The CD activity was assessed by CRP, Crohn's Disease Activity Index (CDAI) and MPV.

Results: This study consisted in 122 patients followed for CD, the median follow-up time was 16 months, 70 (57%) patients were smoking, 15 (12%) had a family history of CD, 52 (42%) had an ileal disease, 36 (30%) a colonic disease and 34 (28%) an ileo-colonic location. CD was inflammatory in 30 (25%) cases, stenosing in 50 (40%) cases, fistulizing in 28 (23%) cases and both stenosing and fistulizing in 15 (12%) cases. Forty five patients (37%) had severe outbreak, 30 (24%) patients a moderate outbreak and 47 (39%) had remission.

The mean CRP was 28 mg / L (15-213), the mean CDAI was 215 (120-412). The MPV value in patients with CD was 8.3 (mean 8.3 fl, 95% CI: 7.92-8.68) and it was significantly lower in this group compared to the HP gastritis group (mean 10.5 fl, 95% CI: 9.25-11.1) with p = 0.04. Otherwise, MPV of active CD (8.1 ± 0.88 fl) were significantly lower than that of inactive CD (8.32 ± 1.02), p < 0.05.

Conclusion: Our study showed that decreased mean platelet volume is an independent laboratory marker of clinical CD's activity. Its use as associated to other indicators allows a better evaluation of the bowel disease inflammation.

Disclosure: Nothing to disclose

P0251

HYPERPHAGIA AND DYSBIOSIS ASSOCIATED WITH JEJUNO-COLONIC ADAPTATION IN A RAT MODEL OF SHORT BOWEL SYNDROME

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Introduction: Short bowel syndrome (SBS), main cause of chronic intestinal failure, results from an extensive resection of small intestine (SI). An improved intestinal absorption and a hyperphagia are critical to reduce parenteral nutrition, and can appear spontaneously over time. Oral nutrition and presence of the colon are two major positive drivers for these adaptations, in which microbiota and gut peptides could play a role.

Aims & Methods: We have developed a SBS rat model to reproduce SBS patient adaptations and study their establishment over 3 weeks.

Wistar rats underwent an 80% resection of SI, ileocecal valve and right colon (SBS) or transection (sham). Survival, weight loss and food intake (FI) were evaluated. Plasma gut hormones were quantified by ELISA. Ki67 Immunostaining was performed on intestinal sections. Expressions of hypothalamic neuropeptides, gut hormones and nutrient transporters, and levels of fecal bacteria DNA were quantified by qRT-PCR. Fecal short chain fatty acids (SCFA) and Lactate were quantified by chromatography or enzymatic reaction. Results are expressed as mean $\pm$ SEM and statistical analyses used non parametric tests.

Results: After 20% of weight loss during the 1st week, SBS rats recovered over the next 2 weeks. At week 1 they exhibited an increased expression of orexigenic neuropeptides (Agrp x3.5, NPY x2 vs sham $P < 0.01$) and started to develop an increase of FI (+70% in SBS vs sham $P < 0.001$). A colonic hyperplasia and an increased production of gut hormones (GLP-2, GLP-1, PYY, Ghrelin) were observed at week 1 (Gillard L. et al. 2016) and preceded jejunal hyperplasia (x1.7 villi height in SBS vs sham $P < 0.01$ at 3 weeks). At week 3, the fecal concentration of SCFAs diminished while L-lactate level greatly increased (55.3 vs 0.3 mMol/g of feces in SBS vs sham $P < 0.001$). The fecal concentration of total bacterial or anaerobic bacteria decreased in SBS rats, while aero-tolerant bacteria increased.

Conclusion: This SBS rat model recapitulates the main adaptations described in SBS adult patients with jejunocolonic anastomosis. The early colonic hyperplasia together with GLP2 increase may contribute to jejunal adaptation. An early rise of orexigenic neuropeptides could explain the hyperphagia in SBS patients. This SBS rat model would allow deep investigations of the gut-brain axis by studying the relationships between changes in hypothalamic neuropeptides, gut hormones, microbiome (or bacterial species) and nutritional status.

References: Gillard L. et al., Sci Rep 2016 PMID: 27323884

Disclosure: Nothing to disclose

P0252

THE INVOLVEMENT OF HYPERPOLARIZATION ACTIVATED CYCLIC NUCLEOTIDE GATED POTASSIUM AND SODIUM CHANNEL 2 (HCN2) IN THE DEVELOPMENT OF ILEUS

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Introduction: Feeding intolerance occurs in approximately 30% of trauma patients resulting in prolonged hospital stays, increased complications, and increased patient care costs. Feeding intolerance is caused by a slowing or cessation of gastrointestinal motility called ileus. Mechanosensitive ion channels play a role in modulating intestinal motility and the response to external stimuli.

Aims & Methods: The aim of the present study was to investigate the role of mechanosensitive ion channels in the development of ileus. Using a microarray to compare small intestinal smooth muscle gene expression in an ileus model versus control, we identified Hyperpolarization Activated Cyclic Nucleotide Gated Potassium and Sodium Channel 2 (HCN2) as being down-regulated in the ileus model. Thus, we investigated the effects of HCN inhibition on intestinal motility. We measured intestinal motility *ex vivo* using an organ bath system. The effects of mechanical stretch and inflammation, which both occur during the development of ileus, were examined. Finally, changes in protein and gene expression for HCN2 were examined.

Results: HCN2 was down-regulated in intestinal smooth muscle after the induction of ileus. Inhibition of HCN channels with ZD7288 (50mM) significantly inhibited agonist-induced (carbachol) contractile activity and calcium sensitivity, but not spontaneous contractile activity, in a dose dependent and tetrodotoxin resistant manner. Increased longitudinal stretch of intestinal tissue lessened the effects of HCN inhibition. Furthermore, increased stretch decreased HCN2 protein levels. Preliminary data show that HCN2 may be down-regulated mostly at the protein level. Conditioned media from stretched macrophages also appeared to attenuate the effects of the HCN inhibitor.

Conclusion: Suppression of HCN2 activity inhibits agonist-induced contractile activity. Both increased stretch, simulating distended bowel, and inflammation appear to attenuate the effects of the HCN2 inhibitor suggesting that HCN2 activity is regulated by increased stretch and inflammatory mediators, both of which are present during the development of ileus.

Disclosure: Nothing to disclose

P0253

THE PHARMACOKINETIC AND PHARMACODYNAMIC RELATIONSHIP BETWEEN APRAGLUTIDE AND CITRULLINE: A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY IN HEALTHY VOLUNTEERS

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Introduction: Plasma citrulline, a biomarker for enterocytic mass, is increased after GLP-2 analog administration.

Aims & Methods: The pharmacokinetic/pharmacodynamic (PK/PD) relationship between apraglutide, a novel long-acting GLP-2 analog in development for short bowel syndrome, and citrulline was evaluated in a randomized, double-blind, parallel arm, placebo-controlled, multiple dose

study. 23 healthy adult volunteers received 6 weekly subcutaneous doses of apraglutide (1, 5, or 10 mg) or placebo and were followed for a further 6 weeks after the last dose. Blood collections were controlled for diet, lifestyle, and diurnal effects. L-citrulline was quantified using a validated LC-MS method. PK data underwent non-compartmental analysis and PD data were analyzed by ANCOVA.

Results: PK parameters indicated a half-life of 72 hours. Increases in citrulline were observed 2 days after the first apraglutide dose and maximal effect was achieved in most subjects after 4 or 7 days. Mean citrulline levels were elevated from baseline in all apraglutide arms and remained elevated during the 6-week treatment period. Citrulline increases were significantly greater with apraglutide 5 mg and 10 mg than with apraglutide 1 mg versus placebo (Table 1). There were no statistically significant differences between 5 and 10 mg apraglutide dose levels. Plasma citrulline levels remained elevated for 10 to 17 days after the final apraglutide dose. Apraglutide was safe and well-tolerated with no serious AEs.

Apraglutide dose (mg)	Difference in citrulline (µg/mL) vs placebo	P-value
1	0.31 [95% CI: -0.4371; 1.0663]	0.3910
5	1.26 [95% CI: 0.5037; 2.0112]	0.0025
10	1.63 [95% CI: 0.8809; 2.3878]	0.0002

[Table 1]

Conclusion: Apraglutide was safe and well tolerated, and displayed a PD response longer than plasma exposure. These PK and PD data confirm the potential for once-weekly subcutaneous dosing of apraglutide and support the continued development of this long-acting GLP-2 analog for the treatment of short bowel syndrome.

Disclosure: Federico Bolognani, Luca Santarelli and Christian Meyer are employees of the study sponsor Pim Gal, Matthijs Moerland, Annelieke Kruithof, Max van Gent are employees of CHDR, which received research funding for study conduct. Pascal Schulthess, Matthias Machacek and Gerard Greig received fees for service during the conduct of the study for service as a consultants.

P0254

SAFETY AND EFFICACY OF APRAGLUTIDE IN PATIENTS WITH SHORT BOWEL SYNDROME: AN OPEN-LABEL PHASE 2 METABOLIC BALANCE TRIAL

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Introduction: Treatment with glucagon-like peptide-2 (GLP-2) analogs promotes intestinal adaptation in patients with short bowel syndrome (SBS). Apraglutide is a novel long-acting GLP-2 analog designed to enable once weekly dosing. This Phase 2 trial investigated the safety and efficacy of once weekly 5 mg apraglutide in patients with SBS intestinal failure (SBS-IF) and intestinal insufficiency (SBS-II).

Aims & Methods: In this open-label trial, 8 adult patients with SBS-IF (n=4) or SBS-II (n=4) and a fecal wet weight of ≥1500 g/day were treated with once weekly subcutaneous 5 mg apraglutide for 4 weeks. Safety was the primary endpoint. As secondary endpoints we examined changes from baseline in intestinal absorption of wet weight, energy (measured by bomb calorimetry) and electrolytes as well as fecal wet weight and urine production using 72-hour metabolic balance studies.

Results: Common treatment-related adverse events were consistent with the physiological effect of GLP-2 and included reduced stoma output (n=6), stoma complication (n=6), nausea (n=5), flatulence (n=4), polyuria (n=3) and abdominal pain (n=3). Once weekly apraglutide significantly increased energy, wet weight and electrolyte absorption, reduced fecal wet weight and increased urine production (Table 1).

	Estimated absolute mean change from baseline (95% CI and p-value, paired t-test)
Wet weight absorption (g/day)	741 (194 to 1287; p<0.05)
Energy absorption (kJ/day)	1095 (196 to 1994; p<0.05)
Fecal wet weight (g/day)	-680 (-1200 to -159; p<0.05)
Urine production (g/day)	560 (72 to 1048; p<0.05)
Sodium absorption (mmol/day)	38 (3 to 74; p<0.05)
Potassium absorption (mmol/day)	18 (4 to 32; p<0.05)

[Table 1. Effects of apraglutide]

Conclusion: 5 mg apraglutide treatment was safe and well tolerated in patients with SBS-IF and SBS-II. For the first time, a once weekly GLP-2 analog significantly improved absorption of wet weight, energy, electrolytes and increased urine production. A phase 3 trial will be initiated to further confirm the efficacy and safety of once weekly treatment of apraglutide.

Disclosure: J. Eliasson: None Declared, M. Hvistendahl: None Declared, C. Meyer Other: Employee of VectivBio AG., F. Bolognani Other: Employee of VectivBio AG., P. Jeppesen Consultant for: VectivBio AG., Speakers Bureau of: VectivBio AG.

P0255

SACCHAROMYCES BOULARDII CNCM-I745 AS AN EFFICIENT PHYSICAL BARRIER TO REDUCE BACTERIAL INFECTIONS: A NEW THERAPEUTIC OPTION?

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Introduction: Antibiotic resistance threatens the effective prevention and treatment of an ever-increasing range of bacterial infections. Development of new therapeutic approaches has become crucial. Among the potential new strategies to reduce or suppress bacterial pathogenicity, the protective effect of a physical barrier can be evaluated.

In the case of *Salmonella enterica* serovar Typhimurium (ST) infection, the bacteria has to approach the intestinal epithelium, move on its surface and invade host cells. During this process, bacterial motility is essential for invasion and pathogenicity. *Saccharomyces boulardii* CNCM-I745 (*S.b*) is a yeast used as probiotic that has been shown to prevent infection by ST and also to affect *in vitro* motility of this pathogenic bacteria (Pontier-Bres R, Plos One 2012). Through experimental and mathematical model approaches this work provides novel hints on how, apart from its pharmacological action, *S. boulardii* CNCM I-745 physically interferes with ST to prevent host cell infection.

Aims & Methods: Study *S.b* as a physical barrier against the bacterial infection.

Phase contrast video microscopy was performed on human colonic T84 cells infected by the *Salmonella* strain 1344 in the presence of *S. b*. The optimized time interval of acquisitions was 0.12 ms, and a manual tracking was performed to study bacteria dynamics (MTrackJ plugin, NIH image J software). Either *S.b* were added together with ST on T84 cells and in this

experimental condition, yeasts are present as single cells. In other conditions T84 cells were incubated over night with yeasts before ST addition. In this case, yeasts formed clusters of several cells: 2, 3 or 4 yeast cells with different shapes. From experimental data, we developed a mathematical model describing the interaction between bacteria, T84 cells and *S.b* as single cells (ST + *S.b* single) or clusters of 2, 3 or 4 *Sb* cells (ST + *S.b* cluster). We performed numerical simulations of the effect of yeasts on bacterial invasion, depending on yeast shape or clusters 'shape'.

Results: Using a data-driven mathematical model, we have shown that, during the first hour after ST inoculation, the introduction of *S.b* has a significant impact on T84 cells invasion. The number of bacteria internalized inside T84 cells decreased, and the estimated number of invading (*i.e.* intra-cellular) bacteria was consistent with the experimentally measured value: up to 10% in case of (ST + *S.b* single) condition and up to 60% or 80% in case of (ST + *S.b* cluster), depending on the number of yeasts in the cluster. Furthermore, our study reveals that rate of the intracellular bacteria depends on spatial arrangement and shape of yeast clusters. These results provide a mechanistic understanding of bacterial pathogenicity suggesting that establishing a physical protective barrier could be a complementary way to fight against bacterial infection.

Conclusion: Physical barrier might be an efficient tool to fight against bacterial infection. In addition to its pharmacological effects, *Saccharomyces boulardii* CNCM I-745 constitutes a physical protective barrier contributing to its efficacy to prevent *Salmonella* infections.

References: Pontier-Bres R., Prodon F., Munro P., Rampal P., Lemichez E., Peyron J-F, Czerucka D. Modification of *Salmonella* Typhimurium Motility by the Probiotic Yeast Strain *Saccharomyces boulardii*. *PLoS One* 2012 7(3): e33796. doi:10.1371/journal.pone.0033796

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P0256

SMALL INTESTINAL BACTERIAL OVERGROWTH REMISSION AND SYMPTOMS IMPROVEMENT AFTER ANTIBIOTIC TREATMENT: A FRENCH RETROSPECTIVE COMPARATIVE STUDY

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Introduction: Small intestinal bacterial overgrowth (SIBO) treatment is usually based on antibiotics with no guideline available.

Aims & Methods: The aim of our study was to investigate the efficacy of different antibiotics in SIBO. A retrospective study was conducted among all patients referred in our center between August 2005 and February 2020. SIBO diagnosis was made using 75g glucose breath test (GBT). Treatment consisted in either a single antibiotic course (quinolone or azole antibiotics) or in a rotating antibiotics course (quinolone alternatively with azole antibiotics) for 10 consecutive days per month for 3 months. A negative GBT after antibiotics was considered as SIBO remission. Quality of life was assessed by GIQLI score before and after treatment. Symptomatic evaluation was realized in simple blind of GBT result: patients were unaware of their results.

Results: A total of 223 patients was included (female 79.8%, mean age 50.2 ± 15,7 years). Remission was observed in 104 patients (46.6%) after one course of antibiotics. Remission was observed more frequently in patients receiving rotating antibiotics than in patients receiving single antibiotic (70.0% vs 50.8%, p=0.05). Remission was associated with a significant improvement in GIQLI score (p=0.03) and in bloating (p=0.004).

Conclusion: In this study, the rotating course of antibiotics was more effective than the single antibiotic course to induce SIBO remission. Remission was associated with improvement in quality of life and bloating. Further randomized studies are needed to confirm these results and to compare rotating antibiotics to rifaximin in SIBO.

Disclosure: Nothing to disclose

P0257

MANAGEMENT OF COELIAC DISEASE PATIENTS AFTER THE CONFIRMATION OF DIAGNOSIS IN CENTRAL EUROPE

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Introduction: Recently, new guidelines for diagnosing coeliac disease (CD) were published by the European Society for paediatric gastroenterology, hepatology and nutrition. However, no recommendation on how the follow-up of CD patients should be arranged are included.

Aims & Methods: The aim of our study was to assess the follow-up practices and experience of CD patients with their follow-up appointments in Central Europe (CE).

Gastroenterologists (GI) and CD patients in five CE countries were asked to complete the web-based questionnaire focusing on CD management practices (diagnostic procedures, regularity of follow-up visits, planned investigations, carried out during the follow-up).

Results: Answers from 147 GI and 2041 coeliac disease patients (60.1% patients, 39.9% caregivers; 80.8% members of patient support groups) from Croatia, Hungary, Germany, Italy and Slovenia were available for the analysis.

More than half of gastroenterologists (58.5%) schedule the first follow-up visit within three months after the confirmation of the diagnosis and 98% within six months. At the follow-up visit, tissue transglutaminase antibodies are checked almost always (95.9%), followed by antiendomysial antibodies (37.4%). Among other laboratory parameters, complete blood

count is always performed in 52.4% of patients. If at the first follow-up visit patient is reporting an improvement, the second follow-up visit is scheduled after 6 or 12 months (41.4% and 34.5% respectively), and when stable, once a year (88.8%). During adolescence, gastroenterologists usually (62.6%) do not increase the frequency of follow-up visits.

At the confirmation of the diagnosis only about two thirds (60.7%) of gastroenterologists refer all of their patients to the dietitian. However, at follow-up visit only 6% refer all their patients and two thirds of gastroenterologists refer less than half.

Paediatric CD patients are usually transferred to adult care at the age of 18 (81.9%). Mostly there is no formal transition (50.3%) or only a written transition report is provided (39.5%).

Among patients, 56.9% of paediatric CD patients and 29.5% adult CD patients have follow-up appointment at least once a year. Almost one third of paediatric and adult CD patients (30.3% and 31.1%, respectively) reported that they have no follow up appointments.

Comparable with the data provided by gastroenterologists, 42.8% of CD patients reported that they had not been appointed to a dietitian. However, among paediatric CD patients, 73.6% were appointed to a dietitian, but on the other hand, less than half (46.3%) of adult patients visited dietitian. **Conclusion:** Follow-up of CD patients is suboptimal. Many patients are not followed despite different reports provided by gastroenterologists. Also, a lot of patients do not have an appointment with the dietitian. The recommendations on the proper follow-up of CD patients together with the proposed investigations are needed in order to improve patient care.

Disclosure: *Study was co-financed by Interreg CE programme (CE 111, Focus IN CD) and ARRS.

P0258

THE KNOWLEDGE ABOUT COELIAC DISEASE AMONG HEALTHCARE PROFESSIONALS AND PATIENTS IN CENTRAL EUROPE

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Introduction: Coeliac disease (CD) is one of the most common lifelong disorders that remains undiagnosed for a long time in many adult and paediatric patients. However, after confirmation of diagnosis, high awareness about the disease is important to avoid disease related complications.

Aims & Methods: The aim of our study was to assess the knowledge about CD among healthcare professionals (HCPs) and patients in Central Europe (CE).

HCPs and CD patients in five CE countries were asked to complete the web-based questionnaire about CD. The questions were divided in subsections on epidemiology, clinical presentation, diagnostics, treatment and follow-up. Achieved scores of different specialists managing patients with CD were compared and regional differences as well as the effect of the duration of the disease and involvement in patient support groups on the patients' knowledge were analysed.

Results: Questionnaire was completed by 1381 HCPs and 2262 CD patients or their caregivers (39% caregivers) from Croatia, Hungary, Germany, Italy and Slovenia. Most participating HCPs were paediatricians (42%), followed by general practitioners (31%). Among CD patients, the majority were members of patient support groups (81%) and 51% were diagnosed within the last 5 years. Mean score achieved by HCPs was 50.8% pts, and by CD patients 56.1% pts, with the highest number of correct answers in both groups found for the treatment and follow-up subsection (Table 1). Paediatric gastroenterologists scored significantly higher (mean 69.2% pts; $p < 0.001$) than internal medicine gastroenterologists, primary care paediatricians (both 54.0% pts) and general practitioners (53.6% pts). Comparing the answers of patients and caregivers, the latter scored significantly higher than adult CD patients (58.3% vs 55.6% pts; $p < 0.001$). There were significant differences in knowledge of patients from different CE regions with German participants scoring the highest (mean 58.3% pts), followed by participants from Croatia and Italy (both 55.6% pts). Members of patient support groups scored higher compared to non-members (mean 57.8% pts vs 53.3% pts; $p < 0.001$) and patients who were diagnosed less than 5 years ago scored higher compared to those diagnosed more than 10 years ago (mean 57.2% pts vs 54.4% pts; $p < 0.001$).

	Overall average	Epidemiology and clinical presentation (mean score)	Diagnostic procedure (mean score)	Treatment and follow-up (mean score)
ALL HCPs (1381)	50.8%	44.4%	36.7%	66.0%
General practitioners (GP) (424)	53.6%	56.7%	40.0%	68.0%
Primary care paediatricians (PrimPed) (405)	54.0%	46.7%	40.0%	68.0%
Paediatric gastroenterologists (PedGI) (49)	69.2%*	61.1%**	63.3%*	81.0%***
Gastroenterologists (GI) (20)	54.0%	52.2%	33.3%	69.0%
All patients (2262)	56.1%	43.0%		73.7%
CD children (63)	53.3%	44.0%		70.0%
Parents (892)	58.3%#	43.0%		76.2%#
CD adults (1307)	55.6%	43.0%		71.2%

[Knowledge of HCPs and CD patients.]

*significant difference vs GP, PrimPed and GI ($p < 0.001$); **significant difference vs GP, PrimPed ($p < 0.001$); ***significant difference vs GP, PrimPed (both $p < 0.001$) and GI ($p < 0.05$)

#significant difference vs CD adults, ($p < 0.001$)

Conclusion: The knowledge about CD among HCPs and CD patients is not satisfactory. It is worrisome that the lowest scores of HCPs were found in the subsection on diagnostic procedures. Further awareness raising and learning activities are needed among HCPs to improve their knowledge and therefore reduce the number of unrecognized patients and unnecessary diagnostic delays.

Also, patients should be better informed about the disease in order to reach higher compliance with the gluten-free diet.

Disclosure: *Study was co-financed by Interreg CE programme (CE 111, Focus IN CD) and ARRS.

P0259

THE INFLUENCE OF CLINICAL PRESENTATION ON GROWTH OF CHILDREN WITH COELIAC DISEASE IN CENTRAL EUROPE

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Introduction: Coeliac disease (CD) can seriously affect nutritional status and growth of children.

Aims & Methods: The aim of our study was to assess the differences in weight and height of symptomatic and asymptomatic children with CD in Central Europe at the time of diagnosis.

An anonymised multi-centre web-based survey was conducted and filled out by paediatric gastroenterologists from five CE countries, providing the data from medical records of CD patients aged < 19 years diagnosed in 2016. Z-scores for weight and height of children with CD at the time of diagnosis were calculated, based on the WHO reference. Differences between symptomatic and asymptomatic patients were assessed.

Results: Data from 653 children (mean age 8 years 3 months (SD±4.5 years); 63.9% female) from Croatia, Germany, Hungary, Italy and Slovenia was available for the analysis. One hundred thirty-four children (20.5%) were asymptomatic at the confirmation of the diagnosis (mean age 8 years 9 months (SD±4 years 5 months), remaining children were diagnosed with CD due to their signs and symptoms (mean age 8 years 1 month (SD±4.5 years). There was no significant difference in age at diagnosis between symptomatic and asymptomatic children.

Slightly more than a quarter (177; 27.1%) of all children belonged to a higher risk group for the development of CD. Among 519 symptomatic children, 88 belonged to the known risk group, mostly having a first-degree family member with CD (73.9%), followed by autoimmune thyroid

disease (15.9%). Among asymptomatic children, 89 belonged to a known risk group, with three quarters (75.3%) having first-degree family member with CD and 15.7% having type 1 diabetes mellitus.

Regarding the growth of children with CD, we found that they had a lower body weight (median z-score for weight for age based on the WHO growth standard: -0.41; min -7.57; max 3.53), whereas their height was equal to the median of the WHO standard (median z-score for height: -0.07; min -5.65; max 7.29). No differences were found between girls and boys.

In Germany, children were shorter compared to children from Hungary and Croatia (median z-score for height: -0.02 and 0.35 respectively; p< 0.05). There were no statistically significant differences in z-scores for height and weight between other countries (Table 1).

	CRO (N=66)	GER (N=69)	HUN (N=381)	ITA (N=83)	SLO (N=54)	CE (N=653)
z-score for weight (median)	-0,04	-0,64	-0,5	-0,13	-0,3	-0,41
z-score for height (median)	0,35	-0,43*	-0,02	-0,2	-0,12	-0,07
*significant vs Croatia and Hungary; p<0.05						

[Median z-score for weight and height of CD patients in CE according to the WHO reference]

Asymptomatic children were slightly heavier and taller compared to the symptomatic children (median z-score for weight: -0.20 and -0.49 respectively, p< 0.05; median z-score for height: -0.11 and 0.16 respectively; p< 0.05) at the confirmation of the diagnosis.

Comparing CD patients from known risk groups, those who were symptomatic (N=88) had slightly lower body mass and were slightly shorter in comparison to asymptomatic CD patients (N=89; median z-score for weight: -0.29 vs -0.23, NS; median z-score for height: -0.09 vs 0.21 respectively; NS).

Conclusion: Children with CD have lower body mass at the time of diagnosis compared to healthy children. Further comparison of asymptomatic and symptomatic patients shows that the growth is significantly more affected in the latter group. These findings stress the importance of early detection of CD before it impairs the growth and further supports the importance of regular screening for CD in risk groups even before the symptoms develop.

Disclosure: *Study was co-financed by Interreg CE programme (CE 111, Focus IN CD) and ARRS.

P0260

CLINICAL PRESENTATION IN CHILDREN WITH COELIAC DISEASE IN CENTRAL EUROPE

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Introduction: During the past decades, there has been a shift in the clinical presentation of coeliac disease (CD) from the historically classical symptoms of malabsorption to now more common non-classical, oligo-symptomatic or even asymptomatic forms.

Aims & Methods: The aim of our study was to assess the clinical presentation of CD in children and adolescents in Central Europe.

An anonymised multi-centre web-based survey was conducted and filled out by paediatric gastroenterologists from five CE countries, providing the data from medical records of CD patients aged < 19 years diagnosed in 2016. Clinical presentation of CD at the time of diagnosis was analysed and the differences in clinical presentation among very young (< 3 years) and older children and adolescents were studied.

Results: Data from 653 children and adolescents (mean age 8 years 3 months (SD±4 years 6 months); 63.9% female) from Croatia, Germany, Hungary, Italy and Slovenia was available for the analysis. One fifth (N=134) of all children were asymptomatic at the confirmation of the diagnosis.

In symptomatic children, the most common leading symptom in every included country was abdominal pain (26.5%). The second most common leading symptom was growth retardation (10.9%), followed by diarrhoea (10.6%) and iron deficiency (8.1%). The majority of symptomatic children (47.6%; N=247) were polysymptomatic, having three or more symptoms, followed by monosymptomatic children (28.5%; N=148). When all symptoms were considered, abdominal pain was the most common (41.2%±9, followed by abdominal distention (25.7%) and diarrhoea (24.3%).

Comparing clinical presentation of CD in very young children (< 3 years) with older children (≥3 years), we found that symptoms and signs of malabsorption were significantly more common in younger (p< 0.001). On the other hand, abdominal pain and asymptomatic presentation were more common in older children and adolescents (both p< 0.001). Some of the most common symptoms are presented in Table 1.

Conclusion: Abdominal pain has become the most common symptom in children with CD, with number of asymptomatic cases increasing in all regions. However, in younger children, symptoms of malabsorption are

still seen very frequently, posing a question what is the reason for the shift in clinical presentation favouring non-classical presentation and asymptomatic disease in late-onset CD.

Disclosure: *Study was co-financed by Interreg CE programme (CE 111, Focus IN CD) and ARRS.

	<3 YEARS OLD (N=74)	≥3 YEARS OLD (N=579)	Sig.
Asymptomatic	6.7%	22.3%	0.001
Abdominal pain	24.6%	56.0%	<0.001
Growth retardation	34.8%	20.0%	0.006
Diarrhoea	52.2%	27.3%	<0.001
Iron deficiency	23.2%	24.2%	0.493
Abdominal distention	56.5%	28.7%	<0.001
Constipation	18.8%	13.1%	0.138
Weight loss	24.6%	7.6%	<0.001
Vomiting	13.0%	5.3%	0.021

[Table 1. Symptoms of CD in children depending on the age.]

P0261

EVALUATION OF GLUTEN IMMUNOGENIC PEPTIDES IN URINE OF CELIAC PATIENTS: A PROSPECTIVE TRIAL

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Introduction: Coeliac disease (CD) is a chronic, immune-mediated small bowel enteropathy and gluten free diet (GFD) represents the only available treatment. Unfortunately, this GFD creates practical, psychological and financial problems and frequently gluten is difficult to avoid due to its widespread use in alimentary products.

Aims & Methods: We aimed to evaluate involuntary gluten contamination in the diet of CD patients.

We conducted a prospective study enrolling treated CD patients attending to our outpatient clinic. Urinary gluten immunogenic peptides (GIP) were determined by means of a lateral flow point-of-care immunoassay (GlutenDetect®; Biomedal S.L., Spain). Celiac Dietary Adherence Test (CDAT), the Milano questionnaire and Visual Analogue Scale (VAS) to evaluate symptoms were tested. Furthermore, the correlation between GIP findings, symptoms and serological status (tissue transglutaminase IgA, tTGA) of the patients were determined.

Results: We enrolled 151 patients (106 female /45 male, 42.2 ± 15.4 years). Among them, we found 22 (33%) (21 female /1 male, 39.6 ± 15.8 years) without demographic differences compared to negative patients. GIP findings was not correlated with neither the CDAT nor the Milano question-

naire in terms of score, being 13.8 ± 4.2 in case of positive GIP vs 13.9 ± 2.3 and 19.8 ± 4.3 vs 19.4 ± 5.3 for CDAT and Milano questionnaire respectively. Moreover, symptoms evaluated by means of VAS did not correlate with the presence of GIP. Neither the general well being was not influenced by GIP findings. Among CD patients, 44 (40 female/4 male, 37.6 ± 14.8) resulted positive to tTGA without declaring a voluntary ingestion of gluten; in case of positive serology, 8 (4%) presented urinary GIP compared to 10 (9.5%) in case of negative tTGA ($p=0.211$).

Conclusion: We found an unexpected presence of urinary GIP in treated and compliant CD patients. GFD Questionnaires do not correlate with “involuntary” gluten ingestions, neither the clinical picture. In case of positive serology we have found a higher prevalence of GIP. This test appears useful in monitoring CD patients although further studies are needed to verify its impact in daily clinical practice.

References: Moreno ML et al. Detection of gluten immunogenic peptides in the urine of patients with coeliac disease reveals transgressions in the gluten-free diet and incomplete mucosal healing. *Gut* 2017;66:250-7

Disclosure: Nothing to disclose

P0262

NEGATIVE DQ2 AND DQ8 CLINICAL LABORATORY RESULTS IN PATIENTS WITH HIGH SERUM TRANSGLUTAMINASE ANTIBODY CONCENTRATIONS

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Introduction: HLA-DQ2 or DQ8 heterodimer molecules contribute to the presentation of gliadin peptides to T lymphocytes and are regarded as essential for the development of coeliac disease (CeD). HLA-DQ typing formed part of ESPGHAN 2012 criteria for CeD diagnosis without histology in symptomatic patients with transglutaminase antibody serum concentrations exceeding 10 times the upper limit of normal ($\geq 10 \times \text{ULN}$ TGA), endomysial antibody positivity (EMA+). HLA-DQ determination is also suggested for the screening of risk persons to exclude CD when the result is negative. HLA-DQ testing has changed in recent years from the laborious and costly traditional typing method to the cheaper detection of DQ2 and DQ8 alleles by their usual single-nucleotide polymorphism (SNP), but this method does not tell which are the alleles exactly when the result is negative.

Aims & Methods: In this study we prospectively evaluated the diagnostic reliability of clinical HLA-DQ testing in patients with high suspicion of CeD. 366 children and adolescents with $\geq 10 \times \text{ULN}$ TGA+ and EMA+ results who were candidates for the no-biopsy diagnostic approach for CeD according to ESPGHAN 2012 criteria were prospectively tested for HLA-DQ2 and DQ8 during 2012-2019. Patients with neither DQ2.5 heterodimers (cis or trans) nor DQ8 were further typed with extended sets of site specific primers (Olerup-SSP, Genovision). In case of still negative DQ result, both serology and HLA typing were repeated from independent blood drawings and small intestinal biopsy was performed. CeD was diagnosed if histology showed Marsh III lesions.

Results: Initial HLA-DQ typing from various accredited clinical laboratories showed no DQ2 or DQ8 heterodimers in 27 of the 366 patients (7.4%), who all were of European Caucasian ancestry. In our testings, eleven of these patients carried the DQB1*0202-DQA1*0201 allele alone, thus half

or the trans DQ2 heterodimer still able to present gliadin in rare cases. In four patients a second blood sample showed DQ2.5 or negative EMA/TGA indicating a sample mix-up at some point during their care. From the remaining 12 patients, 10/10 had Marsh III lesions whose parents consented to biopsy. The most common allele missed by the clinical DQ testing was a variant DQB1*0202 with an A chain DQA1*0303 instead of the conventional DQA1*0201 ($n=5$). The other patients carried variant DQ8 ($n=1$), DQ9 ($n=2$), DQ7 alone ($n=1$) or the DQ5/DQ6 combination ($n=3$).

Conclusion: Variant or non-conventional HLA-DQ alleles do occur in patients with confirmed CeD with villous atrophy and TGA+/EMA+ results, even if rarely. The positive predictive value of high ($\geq 10 \times \text{ULN}$) TGA antibody values for CeD was higher than the negative predictive value of clinical HLA-DQ testing which support the validity of the 2020 modification of the ESPGHAN diagnostic guidelines for CeD. Our results also indicate that formal exclusion of CeD should not rely on a single DQ result, since genetic testing also may have methodological and technical weaknesses.

Disclosure: Nothing to disclose

P0263

THE ADDITION OF DEAMINATED GLIADIN PEPTIDE TO ANTI-TISSUE TRANSGLUTAMINASE ANTIBODIES DOES NOT INCREASE THE LIKELIHOOD OF DETECTING CELIAC DISEASE

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Introduction: The diagnosis of celiac disease (CeD) is based on the presence of specific CeD autoantibodies. Previous studies proposed that the combination of anti-tissue transglutaminase (tTG) IgA and deaminated gliadin peptide (DGP) IgG antibodies increases CeD detection. Recent studies comparing tTG and DGP have shown false positive DGP antibodies in pediatric patients, however this has not been determined in adult populations.

Aims & Methods: Our primary aim was to evaluate whether the addition of DGP antibodies to tTG increases the accuracy of tTG for the diagnosis of adult CeD compared with duodenal biopsy. Our secondary aim was to explore whether the performance of DGP antibodies is kit-dependent. We enrolled consecutive adult patients (>18 years) with suspected CeD attending the celiac clinic at McMaster from January 2017 until December 2019. Participants had both tTG IgA and DGP IgG serology performed at the same time point (within a month), before starting a gluten free diet. Serology kit brand and McMaster vs community lab, was documented for each patient. Upper endoscopy with 6 biopsies from duodenum (2 from D1 and 4 from D2-3) was performed to ascertain diagnosis. Genetic testing (HLA-DQ2 and/or -DQ8) was done in participants with discrepant serology and biopsy results. Statistical analysis was completed using STATA. Sensitivity and specificity was calculated for each test compared to duodenal biopsies and ROC curves were generated with corresponding AUC. Logistic regression was used to assess the likelihood of diagnosing CeD with both serologic strategies. Subgroup analysis was performed to assess the performance of McMaster (local) vs community kits.

Results: One hundred and sixteen patients met the inclusion criteria. From them, 49 and 95 patients were analyzed at the initial and follow up time-points. Overall, there was a low agreement between tTG IgA and DGP IgG at diagnosis and follow up (κ 0.22 and 0.25 respectively). At diagnosis, both tTG IgA and DGP IgG had similar sensitivity compared with duodenal biopsy (86.57% vs 79% $p=0.70$). DGP IgG was significantly less

specific than tTG IgA for the diagnosis of CeD (17% vs 46%; $p = 0.02$). The performance of tTG IgA was superior compared with DGP IgG for the diagnosis of CeD (AUC=0.84 vs 0.49 $p = 0.008$). The likelihood of detecting CeD did not improve with the addition of DGP IgG to tTG IgA (tTG + DGP LR = 26.09 vs tTG LR = 24.51; $p = 0.7$). The performance of tTG IgA alone was better than the combination of tTG IgA + DGP IgG for the diagnosis of CeD (AUC=0.84 vs 0.64; $p = 0.046$). tTG IgA and DGP IgG kits performed differently in detecting CeD as seen in Table 1 (AUC 0.61 vs 0.38).

tTG IgA		DGP IgG	
Kit	AUC (95% CI)	Kit	AUC (95% CI)
McMaster	0.6119 (0.43-0.79)	McMaster	0.6083 (0.311,0.906)
Community	0.8809 (0.77-0.988)	Community	0.3791 (0.125,0.633)
P-value of Fisher's exact test comparing kit types		P-value of Fisher's exact test comparing kit types	
0.045		0.073	

[Table 1. Sensitivity, specificity, and ROC AUC of tTG and DGP serology stratified by McMaster and Community kits]

Conclusion: Overall, tTG IgA outperformed DGP IgG antibodies for the diagnosis of celiac disease. The addition of DGP IgG to tTG IgA antibodies decreased the diagnostic accuracy in patients with normal IgA, possibly related to decreased specificity of DGP. The performance of the test may depend on the type of kit used; however, the preliminary analysis included a low number of cases and should be confirmed in a larger sample size.

Disclosure: All authors have nothing to declare

P0264

TELEMEDICINE IN THE COVID-19 LOCKDOWN: IMPLEMENTATION FROM 0% TO 100% IN AN ITALIAN CELIAC DISEASE-DEVOTED CLINIC

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Introduction: COVID-19 pandemic also had direct effects on traditional healthcare. Celiac Disease (CeD) patients require a lifelong follow-up. At the beginning of the lockdown in Italy, among the others also CeD patients could not reach the GPs or the outpatients' clinic for regular care.

Aims & Methods: The study reports the results of remote consultation offered in the CeD clinic. Between the 9-24 March 2020 we called by telephone all CeD patients in active follow up at the Celiac Disease Centers Units of the University of Salerno (Campania, South Italy) to cancel the planned control visit and to offer remote consultation. We report data of the remote consultation performed from March 9 to May 9 2020.

Results: With the help of all hospital staff, students, and residents we called by phone 611 patients who should have attended the clinic in the next two months 214 patients (mean age 56±4,3 ys) were unable to access remote consultation, of them 62 did not own a cellular phone. Remote consultation was mostly led by telephone and with the help of the GPs. The remaining patients scheduled their visit by WhatsApp video-call in 215 cases, skype video call in 112, other platforms in 70. In the days before the remote consultation, we asked the CeD patients to send via email or WhatsApp the laboratory tests if they had them and to provide the contacts of their GP. In 60 days, we performed 115 remote consultations, free of charge for the patient. The primary needs for consultation were: check of laboratory tests (n. 52), gastrointestinal symptoms (31), psychological imbalance (26, with 4 panic attacks), one case of diverticulitis that was

guided to the Emergency, new-onset constipation (4, 1 of severe constipation), severe hyperglycemia in a diabetic woman. None of the patients attending the clinic suffered from COVID-19.

Conclusion: Remote consultation was not available in our hospital before the COVID-19 pandemic. In the occasion of the COVID-19 crisis we improvised a system of telemedicine adapting the consultation to the digital tools in possession of patients. However, our experience indicates that at least in our region, the access to simple, essential digital tools should be implemented mostly among older people. The majority of patients were happy with remote consultation, grateful and supportive with the team. Our data demonstrate that in an emergency remote consultation, although non-structured, was highly effective in two-thirds of patients.

Disclosure: Nothing to disclose

P0265

DUODENAL BULB BIOPSIES INCREASE THE DETECTION OF VILLOUS ATROPHY WHEN ASSESSING ADHERENCE IN COELIAC DISEASE

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Introduction: Duodenal bulb biopsies have been demonstrated to increase the diagnostic rate of newly diagnosed coeliac disease (CD) by 10%. The aim of this study was to assess the utility of duodenal bulb biopsies for the assessment of established CD.

Aims & Methods: A prospective study of 375 established CD patients (mean age 51.0 years; 69.9% female) who underwent endoscopy for assessment of persisting symptoms or remission at Sheffield Teaching Hospitals was performed, between 2013-2019. Quadrantic biopsies were taken from D2 in addition to duodenal bulb biopsies.

Results: 63.2% (n=137) of patients had ongoing villous atrophy (VA). Table 1 outlines the histological appearance of D1 and D2 biopsies. Among those with VA (n=137), this was confined to D1 in 10.2% (n=14) and to D2 in 8.0% (n=11). There was no significant difference in number of patients with VA confined to D1 versus D2 ($p = 0.69$). There was no difference in age ($p = 0.18$) or gender ($p = 0.10$) between patients with VA confined to D1 compared to the remaining cohort. As time from diagnosis increased, the proportion of individuals with complete duodenal mucosal healing (defined as Marsh 0 in both D1 and D2 biopsies) also increased. Two years after diagnosis 4.9% (n=11) of patients had complete healing, increasing to 10.7% (n=24) after 4 years, 17.3% (n=39) after 6 years, 20.9% (n=47) after 8 years and 24.0% (n=54) after 10 years. A further 11.1% (n=25) of patients achieved complete healing after more than 10 years since diagnosis.

		D1 Histology		
		Normal (Marsh 0)	Marsh 1/2	Marsh 3a-3c
D2 Histology	Normal (Marsh 0)	36.8% (n=138)	3.2% (n=12)	0.5% (n=2)
	Marsh 1/2	5.6% (n=21)	17.9% (n=67)	3.2% (n=12)
	Marsh 3a-3c	1.3% (n=5)	1.6% (n=6)	29.9% (n=112)

[Table 1: Histological appearance of D1 and D2 biopsies]

Conclusion: Duodenal bulb biopsies increased the detection of VA by 10% in established CD, highlighting the importance of bulbar biopsies in established CD. Complete mucosal healing can occur in established CD after a significant delay, suggesting development of immune tolerance in these individuals.

Disclosure: Nothing to disclose

P0266

ARE CELIAC DIETARY ADHERENCE TEST QUESTIONNAIRES AN EFFECTIVE TOOL TO ASSESS ADHERENCE TO A GLUTEN-FREE DIET IN COELIAC DISEASE?

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Introduction: Adherence to a gluten free diet (GFD) in coeliac disease (CD) is challenging, with adherence being reported as 42-91% in the literature. The Coeliac Disease Adherence Test (CDAT) questionnaire is the favoured adherence questionnaire but has never been compared the gold standard of duodenal biopsy (for the presence or absence of villous atrophy).

Aims & Methods: Patients with established CD who were referred for histological assessment of persisting symptoms were prospectively recruited between December 2015 and December 2019. Participants were invited to complete CDAT and Biagi questionnaires and serology at the time of endoscopy. Quadrantic biopsies were taken from D2 in addition to duodenal bulb biopsies. Sensitivities of CDAT, Biagi score and coeliac serology were determined by using the presence (Marsh 3a or above) or absence (Marsh 0-2) of villous atrophy on duodenal biopsy.

Results: 207 patients were prospectively recruited (67.1% female [n=139]). The median duration of GFD (n=200) was 66 months (range= 0-840 months). In total, 31.9% of patients (n=66) had ongoing villous atrophy. Of the patients with villous atrophy, 48.5% were Marsh grade 3a (n=32), 27.3% were Marsh grade 3b (n=18) and 24.2% were Marsh grade 3c (n=16). There was no significant difference in sensitivities between CDAT or Biagi scores and coeliac serology, however CDAT had a significantly greater sensitivity than Biagi score ($p < 0.05$). CDAT had a significantly lower specificity than both Biagi score and coeliac serology ($p < 0.05$). Table 1 outlines the sensitivities and specificities of these tests.

	Sensitivity % (CI)	Specificity % (CI)	Positive Predictive Value % (CI)	Negative Predictive Value % (CI)
CDAT	56.1 (43.3 - 68.3)	51.8 (43.2 - 60.3)	35.2 (29.3 - 41.7)	71.6 (64.7 - 77.5)
Biagi	19.7 (14.1 - 26.9)	94.3 (90.5 - 96.7)	61.9 (41.5 - 78.9)	71.5 (68.9 - 74.0)
CDAT & Biagi	29.7 (15.9 - 47.0)	91.1 (82.6 - 96.4)	61.1 (39.9 - 78.8)	73.5 (69.0 - 77.5)
IgA-EMA	36.4 (24.9 - 49.1)	96.5 (91.9 - 98.8)	82.8 (65.7 - 92.3)	76.4 (72.9 - 79.6)
IgA-tTG	37.9 (26.2 - 50.7)	94.3 (89.1 - 97.5)	75.8 (59.8 - 86.8)	76.4 (72.8 - 79.7)

[Table 1: Comparison of Tools used to assess adherence]

Conclusion: The CDAT questionnaire appears to be a poor marker of villous atrophy, with a similar sensitivity and lower specificity than coeliac serology. Duodenal biopsy remains the gold standard for assessment of adherence in CD, with development of further non-invasive markers required.

Disclosure: Nothing to disclose

P0267

PREVALENCE OF LACTOSE MALABSORPTION IN COELIAC DISEASE AND SYMPTOM CORRELATION

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Introduction: Coeliac disease (CD) is a frequent cause of secondary lactose malabsorption. Many methods are available for the diagnosis of lactose malabsorption. The aim of this study is to assess the prevalence of lactose malabsorption in individuals with CD, as well as symptom correlation with test results.

Aims & Methods: Patients were prospectively recruited between February 2018 and October 2019. Individuals with a potential new diagnosis of CD (positive IgA-EMA/IgA-TTG) or established CD had a duodenal biopsy to assess for lactose malabsorption (Lactose Intolerance Quick Test [LIQT], BIOHIT Oyj, Helsinki, Finland) at time of gastroscopy. Subsequent to this, individuals had a lactose hydrogen breath test (LHBT). Symptoms around the time of gastroscopy were assessed, to allow assessment of symptom correlation with lactose malabsorption (e.g. abdominal pain, bloating, diarrhoea, borborygmi).

Results: 97 patients were prospectively recruited; out of these 24 had a LHBT suggestive of small intestinal bacterial overgrowth (SIBO) and were excluded. Of the remaining 73 patients (n= 54 female, median age = 47 years), 50 patients had a potential new diagnosis of CD and 23 had established CD. The total prevalence of a positive duodenal lactase test was 43.8%, compared to 15.1% for a positive LHBT. The prevalence of lactose malabsorption was significantly higher in individuals with villous atrophy compared to those without, when using the duodenal lactase test ($p < 0.01$). Table 1 highlights the prevalence of lactose malabsorption in each group. There was no significant correlation between symptoms compatible with lactose intolerance detected by either LHBT or duodenal lactase test ($p=1.00$).

	Villous Atrophy (Marsh 3a or above)	No villous atrophy (Marsh 0-II)	Villous atrophy vs no villous atrophy		
	Positive LHBT	Positive Lactase test	Positive LHBT	Positive Lactase test	
Potential new diagnosis of CD (n=39/n=11)	17.9% (n=7)	53.8% (n=21)	0.0% (n=0)	45.5% (n=5)	p=0.32 p=0.74
Established CD (n=4/n=19)	0.0% (n=0)	75.0% (n=3)	21.1% (n=4)	10.5% (n=2)	p=1.00 p=0.02
Total (n=43/n=30)	16.3% (n=7)	55% (n=24)	13.3% (n=4)	23.3% (n=7)	p=1.00 p<0.01

[Table 1: Prevalence of Lactose malabsorption]

Conclusion: The prevalence of lactose malabsorption was higher in individuals with CD using the lactase test compared to the LHBT. The prevalence of lactose malabsorption was significantly higher in those with villous atrophy (VA) compared to those without. Although symptom correlation was poor there may be value in using LIQT when assessing CD patients with persisting symptoms.

Disclosure: Nothing to disclose

P0268

EFFECT OF LOW FODMAP DIET IN WELL TREATED COELIAC PATIENTS WITH PERSISTENT GASTROINTESTINAL SYMPTOMS

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Introduction: Gluten free diet (GFD) usually leads to clinical and histological remission in coeliac disease (CD). However, many patients suffer from persistent gastrointestinal (GI) and/or extraintestinal ailments. These symptoms have considerable similarities with irritable bowel syndrome (IBS), and a diet low in fermentable oligo-, di-, monosaccharides and polyols (FODMAP) is an established treatment for IBS.

Aims & Methods: Our main aim was to study the impact of a low FODMAP diet (LFD) on persistent symptoms in coeliac patients on a GFD.

A randomized controlled trial was performed 2018-2019 in 69 adult patients with biopsy-proven and well-treated CD. Patients were recruited from a web-based national survey. Persistent GI symptoms defined by Gastrointestinal Symptom Rating Scale- IBS version (GSRS-IBS) score ≥ 30 , strict GFD adherence for at least 12 months and serological and mucosal recovery were prerequisites for inclusion. Patients were randomly assigned to LFD in addition to GFD (intervention) or unchanged GFD (control). A clinical dietician instructed patients in the LFD group. Symptoms were measured by GSRS-IBS and Coeliac Symptom Index (CSI) at baseline and at follow up after 4 weeks. Compliance to LFD was self-reported, measured on a scale from 0-100, where 100 means fully compliance. T-test and chi-squared tests were used.

Results: Patients were randomly assigned to LFD (n=33, 29 women, mean age 45.7, SE 2.3) or control group (n=36, 29 women, mean age 44.1, SE 2.1). Mean years since diagnosis was 10.5 years (SD 9.2). Self-reported compliance to a LFD was excellent (score 93.6). At baseline, patients scored highest on the GSRS-IBS domains (mean score ≥ 4) "bloating syndrome" (n=31) and "pain syndrome" (n=20). The total GSRS-IBS score (range 13-91) was 37.0 (12.6) in the control group and 38.9 (10.9) in the LFD group at baseline, and 36.5 (13.7) and 26.8 (12.3) at follow up. Difference between means in the change from baseline to follow in the two groups was 11.6 (95% CI 15.8, 15.8, p<0.001). At baseline the total CSI score was 39.7 (9.8) in the control group and 40.2 (10.2) in the LFD group, and 37.3 (10.1) and 31.6 (9.5) at follow up. Difference between means in the change from baseline to follow in the two groups was 6.1 (95% CI 1.8, 10.4, p<0.001). The number of patients with a CSI score ≤ 30 , i.e. lower disease symptom burden, increased from 4 to 18 (p<0.001) in the LFD group and 7 to 11 (p=0.1) in the control group from baseline to follow up.

Conclusion: LFD in well-treated CD patients with persistent symptoms showed a significant reduction in GI symptoms by GSRS-IBS total score. Lower disease symptom burden was also observed. LFD should be considered implemented in clinical practice for the management of persistent symptoms in CD. However, due to the complexity of LFD in addition to GFD, patients should be followed up carefully.

Disclosure: Nothing to disclose

P0269

ENDOMYSIAL ANTIBODIES POSITIVITY AMONG CHILDREN AND ADOLESCENTS WITH HIGH POSITIVE ANTI-TISSUE TRANSGLUTAMINASE TYPE 2 IGA ANTIBODIES

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Introduction: The European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the Diagnosis of Coeliac Disease recommends that symptomatic patients with positive anti-tissue transglutaminase type 2 IgA (anti-TG2) antibodies levels ≥ 10 times the upper limit of the normal (ULN) values will have the option to omit endoscopy and biopsy in the diagnostic process of coeliac disease (CD), provided anti endomysial antibodies (EMA) are positive in a second blood sample. Since 2016, we used a novel algorithm in the central laboratory of our health maintenance organization, where all blood samples which were tested for CD and were ≥ 10 times ULN in two consecutive tests underwent EMA testing. We aimed to look for the positivity of EMA in this real-life clinical scenario.

Aims & Methods: A retrospective analysis of all anti-TG2 samples which were tested for CD during the years 2016-2018. Our health maintenance organization is the second-largest sick fund in the country, ensuring 25% of the population with a nationwide and representative distribution. Serology samples obtained from all patients countrywide were analyzed in one central laboratory.

Screening serology in all patients started with an anti-TG2 ELISA kit (Phadia, Sweden) after exclusion of Immunoglobulin A (IgA) Deficiency (Defined as IgA< 20mg/dl). EMA testing was done using distal oesophageal primate kits.

Results: During the study period, 124,904 children and adolescents (ages 0-18 years) were tested at least once for celiac serology. There were 3,434 patients with positive anti-TG2 results (2.62% from the overall tested population), 977 (0.75) had IgA deficiency and therefore not tested for anti-TG2. Among patients with positive anti-TG2, 1,382 had an anti-TG2 result ≥ 10 times ULN (1.1%). Eighty-nine patients with anti-TG2 ≥ 10 times ULN were excluded from the final analysis because they had high positive results in the years before the study period.

Overall, 1291 patients had their first anti-TG2 ≥ 10 times ULN during the years 2016-2018. Among them, 534 (41.3%) had a second serology test with results ≥ 10 times ULN and their serum was tested for EMA as well. All of them (100%) had positive results with titers between 1:20 to 1:160 (none below). The rate of patients with high positive serology who underwent endoscopy was 64.3%. There was a difference in the rate of endoscopy between groups; 70.8% of patients who had only one anti-TG2 ≥ 10 ULN as compared to 55.1% among patients who had two high positive tests and an EMA (p<0.001).

Conclusion: In a real-world setting using commercial kits, all children having anti-TG2 levels ≥ 10 times ULN in two consecutive tests had positive EMA as well. This finding suggests that with this kit used, a repeated anti-TG2 of ≥ 10 times ULN may be sufficient rather than ordering an EMA test.

Disclosure: Nothing to disclose

P0270

PROGNOSTIC ROLE OF TISSUE TRANSGLUTAMINASE ANTIBODY IN CELIAC DISEASE

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Introduction: Anti-Tissue transglutaminase antibody (tTGA) is the reference standard for celiac disease (CD) serological screening. Beyond this role, tTGA titer is used during the follow-up of patients to monitor the adherence the gluten-free diet (GFD) or the presence of a complicated disease. However, no clear guidelines are available about the management of patients with persistently positive tTGA during GFD. Aim of this study was to evaluate the features of patients with persistent positive tTGA and their significance.

Aims & Methods: Consecutive CD patients on GFD with persistent positive tTGA levels were enrolled in a single center study, from Jan 2017 to Jan 2020. Antibody titers were evaluated from CD diagnosis to last follow-up. CD diagnosis was based upon the current international guidelines. Clinical features and tTGA levels were recorded each follow-up visit (6-12 months). Urinary gluten-detect test to assess the adherence to GFD, duodenal histology and capsule enteroscopy (CE) to evaluate mucosal status were performed. tTGA + cohort was compared with a control group composed by 212 treated CD patients with negative tTGA.

Results: 65 (12% males, median age at enrollment and CD diagnosis were 37 (14-86) and 31 (1-76), median follow up 4 (1-26) years) patients presented positive tTGA levels during follow up. Roughly, the tTGA levels during follow up were 3 (1-79) folds increased (ULN). Beyond the titer, 4 different tTGA trends were recognized: I) 36 (55%) patients with a progressive titer decrease during 3 (1-13) years of follow-up with 8 negativization after 2-13 years after diagnosis; II) 16 (25%) patients with a fluctuating behavior during 7 (1-26) years of follow-up. In 50% of cases, antibodies turned negative at least once; III) 3 (5%) patients with an increase in the titer [12 (2-19) years of follow-up]; IV) 10 (15%) Patients who had a steadily increased titer during 9 (4-14) years of follow-up.

Compared to the controls, the tTGA+ patients did not present a different age at diagnosis and autoimmune comorbidities (20% vs 25%). The duodenal histology profile of the groups evidenced the presence of atrophy in 10 % and 36% in tTGA positive and negative groups, respectively ($p < 0.005$).

Gluten detection resulted positive in three (8%) cases.

In the tTGA+ group, 24 patients underwent capsule enteroscopy and in 42% a mucosa atrophy was detected mainly in the proximal part of the small bowel, but in most of the cases atrophy was not confirmed histologically.

Conclusion: tTGA positiveness during CD follow up did not presented a relevant clinical significance without association with autoimmune comorbidities and mucosal damage. Patients with corrected GFD and tTGA + without warning symptoms, can be followed without increasing the number of invasive procedures.

Disclosure: Nothing to disclose

P0271

SAFETY AND PHARMACOKINETICS OF THE GUT-SELECTIVE JANUS KINASE 3 COVALENT INHIBITOR TD-5202 IN HEALTHY SUBJECTS

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Introduction: TD-5202 is a covalent irreversible Janus kinase 3 (JAK3) inhibitor designed for oral administration. JAK3 is central to multiple inflammatory cytokine signaling cascades. TD-5202 was designed to be gut-selective by having limited oral absorption and rapid systemic clearance to minimize the potential for systemic adverse events (AEs). Several types of inflammatory intestinal disorders may be amenable to treatment with TD-5202, including celiac disease, ulcerative colitis, Crohn's disease, drug-induced colitis, and intestinal graft versus host disease.

Aims & Methods: A first-in-human, randomized, double-blinded, placebo-controlled, single and multiple ascending dose (SAD and MAD) study was conducted in 56 healthy subjects to evaluate the safety, tolerability, and pharmacokinetics of TD-5202. Subjects were randomly assigned to receive one of the following treatments as 100-mg TD-5202 or matching placebo capsule(s): 100, 300, 1000 or 2000 mg TD-5202 single dose (SAD), and 100, 300, or 1000 mg twice daily (BID) (total daily doses of 200, 600 or 2000 mg) for 10 days (MAD). Safety was monitored through physical examinations, vital signs, 12-lead ECGs, clinical laboratory tests, and assessment of AEs. Serial blood samples were collected prior to and following the dose on Day 1 (SAD and MAD) and on Day 10 (MAD) to determine the plasma concentration of TD-5202. Urine for the determination of TD-5202 concentration was collected in the SAD cohorts at various post-dose intervals.

Results: Thirty-two subjects (16 male, 16 female) with mean (range) age of 35 (19-55) years and body weight of 74 (53-111) kg participated in the SAD study. Twenty-four subjects (20 male, 4 female) with mean (range) age of 34 (20-52) years and body weight 83 (66-109) kg participated in the MAD study. No serious AEs were reported in either the SAD or MAD cohorts. All reported treatment-emergent AEs were mild in severity. Three AEs (out of 25 reported in 13 of 32 subjects) in the SAD cohorts and 1 AE (out of 25 reported in 10 of 24 subjects) in the MAD cohorts were considered related to study drug: diarrhea, abdominal discomfort, and vomiting (2000 mg, SAD), and abdominal pain (placebo, MAD). No clinically significant changes from pre-dose baseline in laboratory assessments (in particular lipid, coagulation, hematology and natural killer cell counts), vital signs or ECGs were observed at any time point post-dose in either the SAD or MAD cohorts. Plasma TD-5202 concentrations were low (< 35 ng/mL) following single oral doses up to 2000 mg and multiple doses up to 1000 mg BID. Exposure (AUC and C_{max}) increased in a slightly less than dose-proportional fashion across the studied single-dose range, and dose proportionally after multiple-dose administration. Drug accumulation after BID dosing averaged between 2.5- and 2.9-fold. Steady state was attained within 4 days of repeated dosing. The mean terminal elimination half-life was independent of dose, ranging from 15 to 20 hours after single or repeat dosing. Urinary excretion of TD-5202 was low ($< 0.2\%$) at all single-dose levels.

Conclusion: TD-5202 was generally well-tolerated as a single dose up to 2000 mg and as multiple doses up to 1000 mg BID for 10 days. Consistent with a gut-selective approach, steady-state systemic exposures of TD-5202 at the highest tested dose (1000 mg BID) were low with mean C_{max,ss} (13 ng/mL) approximately 11-fold below the protein-adjusted JAK3 IC₅₀ (150 ng/mL), which was measured in human CD4+ T cells as inhibition of IL-2/anti-CD3 phosphorylation of STAT5.

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P0272

DUODENAL HISTOLOGICAL FINDINGS AND RISK OF CELIAC DISEASE IN SUBJECTS WITH AUTOIMMUNE ATROPHIC GASTRITIS: A RETROSPECTIVE EVALUATION

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Introduction: Autoimmune atrophic gastritis (AAG) is a multifaceted disease characterised by a variable spectrum of gastric and extra-gastric symptoms. AAG has been associated with other autoimmune diseases, particularly autoimmune thyroid diseases, while it is still unknown whether these patients have a higher risk of celiac disease (CeD) or of any other particular duodenal histologic damage.

Aims & Methods: Our study aimed at evaluating the duodenal histological findings and the risk of CeD in patients with AAG, with and without other concurrent autoimmune diseases. We retrospectively collected all the histologic findings of the adult patients undergoing upper gastrointestinal endoscopy with concurrent duodenal and gastric biopsies at our endoscopy unit between 2015-2018 and regularly followed at our centre. Date of endoscopy evaluation, endoscopy indication, data on previous CeD diagnosis and other autoimmune associated diseases, and a full description of histological diagnosis were recorded. Categorical variables were expressed as numbers and percentages, whereas continuous variables were expressed as mean $\pm$ Standard Deviation (SD). Chi-square analysis was used to compare categorical variables while t-test was used for continuous. A p value < 0.05 was considered statistically significant. STATA 11 was used for statistical analysis.

Results: Of the 2423 evaluated endoscopies, 209 patients had an AAG diagnosis (8.6%). One hundred-thirty-nine patients, aged 57.4 (SD 13.2) years, were regularly followed at our centre and were enrolled in the study. Overall, five subjects with CeD among the AAG patients were identified (3.6%), aged 56.7 years old (SD 11.3) and all females. Four patients (2.9%) had already received a CeD diagnosis at the time of the endoscopy considered for the study and therefore were on a gluten free diet, while one (0.7%) was diagnosed at the time of the study. Looking at the possible association with other autoimmune diseases, we identified 2 cases of CeD in subjects with only AAG (2/57, 3.5%) vs 3 cases in those presenting at least one other autoimmune disease (3/82, 3.7%), the difference being far from statistically significant ($p=0.9$). The new CeD patient had a histological damage compatible with Marsh 3, while those on gluten free diet had a Marsh 0 in three cases and a Marsh 1 in one. Considering only patients with AAG but no CeD, we observed that most of them had a Marsh 0 (92.5%), while 6% had a Marsh 1 duodenal histology. Two patients had a villous atrophy without any increase of intraepithelial lymphocytes (IEL): one was a 85 years old female with HCV-related cirrhosis with an increase in eosinophilis and mastcells in the *lamina propria* and was treated with olmesartan, the second was a 75 years old female with familiarity for inflammatory bowel disease.

Conclusion: AAG patients who undergo regular upper endoscopy follow-up should be evaluated at least once with duodenal biopsies. This is true both in patients with AAG as a single autoimmune disease and in those with multiple associations such as in autoimmune polyendocrine syn-

dromes. In absence of other specific clinical and biochemical suspicious data, a CeD serology should be prescribed only in those with duodenal histologic damage. The findings of an isolated IEL or villous atrophy in AAG are not exclusively related to CeD and alternative causes should be looked for.

Disclosure: Nothing to disclose

P0273

DUODENAL TRANSCRIPTOMIC ANALYSIS CAPTURES HETEROGENEITY WITHIN COELIAC DISEASE PATIENTS

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Introduction: Active coeliac disease is characterized by villous atrophy of the small-intestine, with crypt hyperplasia and influx of intra-epithelial lymphocytes. Despite a common histological picture, the pathways leading to tissue destruction may vary across CeD patients as suggested by epidemiological, clinical and immunological data. A better understanding of the factors driving the heterogeneity within coeliac patients are crucial to further understand disease pathogenesis and identify potential therapeutic approaches.

Aims & Methods: In this study we aimed at investigating the duodenal transcriptional signature of active coeliac disease patients to investigate disease heterogeneity and identify novel pathways involved in disease development. Duodenal biopsies were collected from n=48 patients with coeliac disease at diagnosis, and n=45 non-coeliac controls during upper-endoscopy. Subsequently, RNA and DNA were extracted from the whole biopsy, cDNA libraries were prepared and sequenced on HiSeq Illumina 4000. Genotype data was generated by Global Screening Array. All patients were enrolled at the University of Chicago and the study protocol was IRB approved.

Results: We applied principal component analysis (PCA) over the transcriptomic profile revealing a considerable transcriptional difference between active celiac and healthy biopsies. Next, to further explore heterogeneity within coeliac disease subjects, we performed a PCA on only the biopsies of active coeliac subjects. Then, we calculated the ratio of the APOA4 and Ki67 genes (a proxy for villous-to-crypt-height)¹, applied a cell-type² and a KEGG pathway enrichment scores, to possibly explain the heterogeneity captured by the PCs. In our dataset, APOA4/Ki67 ratio was highly correlated (Pearson $P=1.4 \times 10^{-15}$, $R = 0.87$) with PC1, implicating tissue destruction as the main source of transcriptional heterogeneity among active celiac disease patients. Accordingly, celiac biopsies with more tissue destruction clustered further away from controls. Moreover, a PC1 score that is associated with lower villus-to-crypt-height (lower APOA4/Ki67 ratio), was also significantly associated with more CD4+ T-cells, less macrophages as assessed using a deconvolution approach and associated to a distinct immunological signature.

Conclusion: Combining PCA and multiple enrichment tools over duodenal transcriptional data, we revealed a significant heterogeneity in biopsies of active coeliac disease patients that reflects a spectrum of histological severity and distinct immunological signature. Unveiling disease heterogeneity will help a better understanding of disease etiopathogenetic events and allow future personalized preventive or therapeutic strategies.

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Disclosure: Nothing to disclose

P0274

A FAMILY HISTORY OF AUTOIMMUNITY IS A RISK FACTOR FOR CELIAC DISEASE AND JUVENILE IDIOPATHIC ARTHRITIS CO-OCCURRENCE

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Introduction: Autoimmune disorders share common predisposing factors and immune pathogenic mechanisms. The prevalence of celiac disease (CD) has been reported to be consistently higher in patients with juvenile idiopathic arthritis (JIA) in comparison to the general population, however not negligible variations in the prevalence have been observed in distinct geographic locations (1-4).

Aims & Methods: In order to investigate the co-occurrence of JIA and CD in southern Italy and to identify potential predisposing factors, we conducted a single-center retrospective study. All patients diagnosed with JIA according to International League of Associations for Rheumatology criteria, admitted to the Pediatric Rheumatology Unit of the University of Naples Federico II from January 2001 to December 2019, were included. For each patient, demographic, clinical and laboratory data were extracted from clinical charts. Differences between patients affected by JIA with or without CD were analysed.

Results: Three hundred twenty-nine JIA patients (246 females, 83 males; median age 12.5 years, IQR 9.1-16.1) were included in our study. Median age at JIA onset was 4 years (IQR: 2.2-7.8). Eight patients (2.4%) received a diagnosis of CD. Five were diagnosed according to the ESPGHAN guidelines. Two were diagnosed solely based on positive serology that normalized after the beginning of the gluten-free diet (GFD). One patient received a diagnosis of Potential CD (positive serology in the absence of villous atrophy). All of them started a GFD. Only in one patient CD onset preceded JIA, that occurred despite the GFD. The remaining seven developed JIA first. Most of those (5/7, 71.4%) were asymptomatic and diagnosis followed the screening for CD that all JIA patients undergo in our clinic. In our cohort the prevalence of CD was higher than that reported in the general population (2.4% vs 1%, $p < 0.05$). No differences were observed in regard to JIA subtype and ongoing treatment for JIA ($p = 0.646$) between patients with or without CD. Notably, 87.5% patients with JIA and CD had at least one family relative with an autoimmune disorder compared to 45.8% of those without CD ($p < 0.05$). In none of those patients GFD promoted clinical improvement, nor prevented JIA relapse. Indeed, five patients required a new disease modifying antirheumatic drug (DMARD). Finally, 87.5% patients with JIA and CD required both a conventional DMARD and a biological DMARD (bDMARD) over time compared to 34.3% of those without CD ($p = 0.004$).

Conclusion: A higher prevalence of CD in patients with JIA was found in our wide southern Italian cohort in comparison to the general population. Notably, a positive family history of autoimmunity was found to be associated with a higher co-occurrence of JIA and CD, suggesting that common predisposing factors shared across autoimmune disorders may contribute to both diseases.

Furthermore, our patients with JIA and CD more frequently required a bDMARD than patients without CD, suggesting that JIA course can be more aggressive in children with CD. Our findings support the need for an active screening for CD in patients with JIA, especially in those with a positive family history of autoimmunity. This is clinically relevant since the clinical course seems to be more aggressive in these patients and require a step-up therapy.

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Disclosure: Nothing to disclose

P0275

DISEASE BURDEN AND QUALITY OF LIFE IMPACTS IN PATIENTS WITH CELIAC DISEASE ON A GLUTEN-FREE DIET: AN ANALYSIS OF THE ICURECELIAC REGISTRY

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Introduction: A gluten-free diet (GFD) is the only treatment option currently available to celiac disease (CeD) patients, however, response to a GFD is highly variable. This study aimed to identify patient subgroups with distinct CeD symptom burden profiles and describe the corresponding characteristics, impact of CeD on quality of life (QoL), and the effectiveness of a GFD among patient subgroups.

Aims & Methods: A cross-sectional study of US patients with CeD in the iCureCeliac® registry between Dec 2015 to Oct 2019 was conducted. Inclusion criteria for this analysis were: patients reporting biopsy-confirmed CeD and those with complete Patient-Reported Outcomes Measurement Information System-Gastrointestinal symptom (PROMIS-GI) and Celiac Symptom Index (CSI) questionnaire data. Patient subgroups with distinct CeD symptom burden profiles (as measured by multiple domains) were identified using latent class analysis (LCA), a statistical method for identifying distinct unobserved groups. Patient responses to the PROMIS-GI and CSI questionnaires were used to define the CeD symptom burden subgroups in the LCA model. Patient demographics (age, gender), CeD characteristics (age at diagnosis, duration of disease), QoL (Celiac Disease Quality of Life Measure [CD-QOL]), health status (36-Item Short Form Health Survey [SF-36]), and self-reported adherence to a GFD were assessed for the overall study population and for LCA-defined subgroups. Descriptive statistics were calculated for the overall patient population and compared between subgroups.

Results: Of 5690 patients in the iCureCeliac[®] registry, 382 were eligible for inclusion, most of whom were female (82.5%), and the mean (SD) age was 40.9 (18.0) years. Mean (SD) age at CeD diagnosis was 35.7 (17.3) years and duration of CeD 5.1 (6.9) years. Most patients (93.2%) reported “always” maintaining a strict GFD, although almost half (46.9%) reported CeD symptoms despite adherence to a strict GFD.

The LCA identified two distinct subgroups: patients with a lower CeD symptom burden profile (n=180) and patients with a higher CeD symptom burden (n=202). In general, patient demographics and CeD characteristics were similar between subgroups, and there were no differences in self-reported adherence to a GFD ($p=0.902$). Compared with patients with lower symptom burden, patients with higher symptom burden: 1) were more likely to report CeD symptoms despite self-reported adherence to a GFD (66.7% [n=116] vs. 29.2% [n=57]; $p<0.001$; overall 46.9% [n=173]); 2) were less likely to report a GFD effective for treating their most significant CeD symptoms (31.1% [n=52] vs. 60.9% [n=106]; $p<0.001$; overall 46.3% [n=158]); 3) had worse CeD-related QoL and general health status ($p<0.05$ in CD-QoL and all SF-36 components) and 4) had a higher mean (SD) number of days per year absent from school or work due to gluten exposure (45.7 (102.2) days vs. 16.7 (63.0) days; $p<0.05$; overall 32.1 (87.1) days) or gluten-related disorders (29.5 (74.0) days vs. 10.3 (39.8) days; $p<0.05$; overall 21.0 (61.8) days).

Conclusion: This study indicates that while most patients with CeD report adherence to a GFD, many still experience CeD symptoms, and their condition had a substantial impact on their day-to-day lives. These observations were more pronounced in patients with higher symptom burden, although findings were similar among patients with lower CeD symptom burden. These data underscore the heterogeneity of celiac disease burden and highlight the need for therapeutic options beyond GFD to mitigate disease burden in all patients with CeD.

Disclosure: Kristina Chen was an employee of Takeda Pharmaceuticals Inc. at the time of the research. Marilyn Geller is an employee of Celiac Disease Foundation, a nonprofit organization that received funding from Takeda to conduct this study. Daniel Leffler is an employee of Takeda Pharmaceuticals Inc. Lisa Meckley is an employee of Takeda Pharmaceuticals Inc. Fan Mu is an employee of Analysis Group, Inc., a consultancy that received funding from Takeda to conduct this study. Kalé Kponee-Shovein is an employee of Analysis Group, Inc., a consultancy that received funding from Takeda to conduct this study. Elyse Swallow is an employee of Analysis Group, Inc., a consultancy that received funding from Takeda to conduct this study.

P0276

COELIAC DISEASE - VALUE OF SEROLOGY IN PREDICTING MUCOSAL RECOVERY

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Introduction: Coeliac disease (CD) is an immune-mediated disorder that affects the small bowel in genetically predisposed individuals precipitated by the ingestion of gluten¹. The majority of deleterious health consequences of CD are most likely to be secondary to intestinal inflammation². Hence, mucosal recovery is a desirable goal of therapy. However, the majority of guidelines do not recommend an absolute need for performing routine follow-up biopsy for all patients^{1,3-6}. In fact, routine re-biopsy to assess response to diet is still controversial and serological response is often

used as a surrogate for histological recovery. The aim of the present study was to assess whether serology is capable to predict mucosal healing and refine adequate follow-up of patients with CD.

Aims & Methods: We collected data retrospectively (between January 2010 and January 2020) from adult coeliac patients under a gluten-free diet for at least two years and with negative serology (anti-tissue transglutaminase 2 IgA or IgG < 7 UI/L), who were submitted to a follow-up upper endoscopy with duodenal biopsies. At the endoscopy, biopsies were performed on the bulb and on the second duodenal portion, placed in separate vials. Histological evaluation was performed by anatomopathologists dedicated to the gastrointestinal tract and the result was expressed according to the Marsh classification. Histological remission was considered if Marsh 0 was reported.

Results: A total of 77 seronegative patients underwent a follow-up upper gastrointestinal endoscopy. Overall, the median time to duodenal biopsies was 62 months (range 1-187 months) after the antibody became negative. Most individuals were females (81,8%) and with a median age of 34 years old (interquartile range 23-45 years). Macroscopic features, namely mucosal fissuring, bulb atrophy or scalloping of mucosal folds, were detected in 27 (35,1%) patients. With regard to histological changes, only 54 (70,1%) individuals achieved complete normalization of the mucosa, that is, normal villous and crypts height with no evidence of intraepithelial lymphocytosis (Marsh 0). Although it was not possible to select an appropriate cut-off value to predict active intestinal inflammation within patients with seronegative status, those with the highest levels of serum tissue transglutaminase antibodies were more significantly associated with persistent histologic activity (2,1 vs 1,3 UI/L, $p=0,04$).

Conclusion: Serology appears to be a poor predictor of small-bowel healing. In fact, histological activity is present in about 30% of patients with negative serology. Given the high prevalence of this condition worldwide, we suggest performing a follow-up biopsy in seronegative adults at least two years after starting gluten-free diet to assess for mucosal healing, especially in patients with antibodies titers in the upper limit of normal values. With this procedure, we may be able to identify those requiring more intensive clinical management.

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P0277

SYMPTOMS AND BIOMARKERS ASSOCIATED WITH UNDIAGNOSED CELIAC DISEASE

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Introduction: Studies have indicated that underdiagnosis and diagnostic delay are common in celiac disease. Therefore, it is important to increase our knowledge of what symptoms and biomarkers could identify undiagnosed cases of celiac disease. We aimed to investigate whether undiagnosed celiac disease is associated with specific symptoms or biomarkers.

Aims & Methods: We screened for celiac disease antibodies in stored blood samples from 16,776 participants in eight population-based studies examined during 1976-2012. A case of undiagnosed celiac disease was defined as celiac disease antibody positivity without a known diagnosis of celiac disease in the National Patient Register. Celiac disease antibody positivity was defined as IgG-deamidated gliadin peptide above 10.0 U/mL and/or IgA-tissue transglutaminase (TTG) or IgG-TTG above 7.0 U/mL. In all studies general health symptoms were recorded by participant questionnaire, including self-perceived health, tiredness, headache and gastrointestinal symptoms. Furthermore, blood samples were drawn for analyses of biomarkers e.g. hemoglobin, blood glucose, cholesterol, liver parameters and vitamins. The participants with undiagnosed celiac disease were matched by sex, age and study with four controls among the celiac disease antibody negative participants.

Results: 5 participants with known celiac disease in the National Patient Register were excluded, resulting in a population of 16,771 participants. In this population 1% (169/16,771) had undiagnosed celiac disease. There were no statistically significant differences in symptoms between cases and controls. Undiagnosed celiac disease was associated with low blood cholesterol (< 5 mmol/L) and low hemoglobin (< 7.3 mmol/L for women and < 8.3 mmol/L for men).

Conclusion: In this general population study, undiagnosed cases of celiac disease did not have more symptoms than controls. Decreased levels of cholesterol and/or hemoglobin in the blood were associated with undiagnosed celiac disease.

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P0278

COHORT-BASED COELIAC AUTOIMMUNITY AMONG DANISH ADOLESCENTS

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Introduction: The prevalence of coeliac disease (CD) has been increasing in the Western world. The prevalence of diagnosed CD in Denmark is 0.18% in adults and 0.12% in children and adolescents. However, it is presumed that only 1 in 10 adults are diagnosed.

The aim of this study is to estimate the prevalence of CD in Danish adolescents and, in the long term, to establish a cohort to identify risk factors for the development of CD with a focus on the gut microbiota.

Aims & Methods: The study addresses an unselected cohort of 7432 children and adolescents (15-22 years of age) from the Island of Funen, Denmark. The participants are a subsample of the Danish National Birth Cohort, with a total of approx. 100,000 participants, who have been followed from their mother's pregnancy.

The participants in this ongoing study are invited to a clinical visit through an invitation in their digital mailbox followed by a written letter. The visit consists of measurement of height, weight, blood pressure, a blood sample and a buccal swap.

For microbiome analysis, the participants hand in a frozen faecal sample, which they have prepared at home. In addition, the participants fill in a questionnaire on symptoms of CD, family history and gluten ingestion. CD diagnosis is based on positive IgA transglutaminase antibodies (TTG IgA) at screening, confirmed by duodenal biopsies compatible with CD (Marsh 2-3). CD autoimmunity is defined as TTG IgA above the upper limit of normal.

We calculate the minimum prevalence of CD as the number of CD cases diagnosed before and during this study out of all invited participants and the study cohort prevalence of CD as the number of CD cases diagnosed before and during the study out of all examined participants.

Results: So far, we have invited 7432 participants, of whom 1443 have accepted our invitation, resulting in a participation rate of 19%. We have investigated 1112 participants, 64% (708/1112) were females. 14 participants had CD diagnosed before the study. In total, 32 participants had TTG IgA above the upper limit of normal including three participants with known CD. 11 participants had TTG IgA at ten times or higher the upper limit of normal.

Regardless, all were a- or oligosymptomatic. So far, duodenal biopsies are available for 22/29 participants and 15 of these (68%) had biopsies compatible with CD. Among these, eight had TTG IgA at ten times or higher the upper limit of normal. Three participants refused a gastroscopy.

They were retested with negative endomysial antibodies and a CD diagnosis was dismissed. The minimum prevalence of CD was 0.4% ((15+14)/7432). The prevalence of CD in the study cohort was 2.6%-3.0% ((29-33)/1112) depending on CD diagnosis in the four participants positive for TTG IgA with no biopsies yet available. The minimum prevalence of CD autoimmunity was 0.4% (29/7432) and the prevalence of CD autoimmunity in the study cohort is 2.6% (29/1112).

Conclusion: Regardless that this may be a selected sample, our study suggests that CD autoimmunity and CD is more common than expected among Danish adolescents.

Disclosure: C. Crawley have received a research grant from Thermo Fischer A/S, they have no influence on the study design.

P0279

A MULTICENTRE STUDY OF SMALL BOWEL CAPSULE ENDOSCOPY IN REFRACTORY COELIAC DISEASE - A LUXURY OR A NECESSITY?

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Introduction: Small bowel capsule endoscopy (SBCEs) has an established role in the management of refractory celiac disease (RCD) to detect complications. The aim of this study was to define the role of SBCE at diagnosis and investigate its impact on management during the course of RCD.

Aims & Methods: Patients with histologically confirmed RCD who underwent successive SBCEs were recruited retrospectively from two tertiary centres for the management of celiac disease (CD). Macroscopic features of CD and extent of disease on sequential SBCEs were analysed.

Results: Sixty patients with RCD (median duration of CD of 23 months) were included.

Percentage extent of affected small bowel (SB) mucosa improved on repeating a second SBCE in 26 patients (49.1%) (median 27.6 vs 18.1%, $p=0.007$). However, the improvement was not sustained in subsequent SBCEs.

Patients with RCD type II had more extensive disease than those with RCD type I on first (41.4 vs 19.2%, $p=0.004$) and second (29.8 vs 12.0%, $p=0.016$) SBCE. Patients with RCD type I tended to show greater improvement in percentage of abnormal SB involved on repeat SBCE, compared to the RCD type II ($p=0.049$).

There was no correlation between percentage of abnormal SB mucosa and endomysial antibody and tissue transglutaminase antibody at first ($p=0.696$, $p=0.662$) and second SBCE ($p=0.180$, $p=0.790$).

Histology did not correlate with percentage of abnormal SB mucosa at first SBCE ($p=0.434$) but there was a degree of correlation at second SBCE ($p=0.001$).

Nine patients (15%) had RCD-related complications. Five patients developed ulcerative jejunoileitis, three patients developed EATL and one patient developed cutaneous T cell lymphoma.

Conclusion: SBCE can be a useful tool to monitor the effects of treatment primarily following initiation of treatment. Patients with RCD type II have more extensive SB disease equating to a more aggressive disease pattern.

Disclosure: Nothing to disclose

P0280

SHOULD DUODENAL BIOPSY STILL BE A PREREQUISITE FOR THE DIAGNOSIS OF COELIAC DISEASE IN ADULTS? AN ANALYSIS OF THE DIAGNOSTIC UTILITY OF SEROLOGY

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Introduction: The pediatric guidelines support the use of the 'No Biopsy Approach' in the diagnosis of coeliac disease. However, histological evidence of villous atrophy remains the gold standard for the diagnosis of coeliac disease in adults.

Aims & Methods: We aimed to evaluate if a positive IgA anti tissue transglutaminase (IgA anti TTG), at a titer >10 times the upper limit of normal (ULN) in an addition to a positive endomyseal antibody (EMA), could predict histological evidence of coeliac disease. Specifically, we aimed to look at this in our adult population and determine if the degree of accuracy is equivalent to that observed in the paediatric population. The elimination of a requirement for gastroscopy would likely be more acceptable to the patient and would expedite the diagnosis of coeliac disease.

Following ethical approval, a retrospective cohort study was performed. Newly diagnosed coeliac patients between 2015 - 2018 were identified. Patients with selective IgA deficiency or those who had started a gluten free diet before D2 biopsy were eliminated from the analysis. All biopsies were reclassified according to the Marsh classification, performed by two independent pathologists who were blinded to the anti TTG titre.

Results: 173 cases of newly diagnosed coeliacs were identified, over a 3 year period, on the basis of positive serology and histology. 25% ($n=43$) of these had an IgA anti TTG > 10 times the ULN, and a positive EMA. Of this cohort, 96% ($n=41$) had an OGD with D2 biopsies. Histology revealed a Marsh classification of 3b or higher in 97%, with no patient having a Marsh of 0 or 1. The median amount of biopsies taken at diagnosis was 5. Interestingly 96% of those with anti TTG > 6 times the ULN and a positive EMA who were biopsied had findings consistent with Marsh 3 and above.

Conclusion: The positive predictive value of having an anti TTG > 10 the ULN and a positive EMA, in the diagnosis of coeliac disease, is 1 in our cohort. We propose that the histological confirmation of coeliac disease is unnecessary.

We hope that such a proposal should be welcomed by patients and physicians who are seeking alternatives to aerosolized procedures during the current medical climate.

Disclosure: Nothing to disclose

P0281

COMPARISON AND PERFORMANCE CHARACTERISTICS OF SERUM BIOMARKERS TO EXCLUDE THE DIAGNOSIS OF BILE ACID MALABSORPTION IN PATIENTS WITH CHRONIC DIARRHEA

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Introduction: Bile acid diarrhea (BAD) is a common condition when excessive bile acids (BAs) enter the colon due to bile acid malabsorption (BAM). Impaired metabolism of BAs interaction is involved in the pathophysiology of chronic diarrhea due to microscopic colitis (MC), irritable bowel syndrome (IBS-D) and inflammatory bowel disease (IBD).

Aims & Methods: The aim is to investigate the diagnostic accuracy of 7- α -hydroxy-4-cholesten-3-one (C4) and fibroblast growth factor-19 (FGF-19) as biomarkers for BAM. We enrolled consecutive 109 adult patients with chronic diarrhoea and 11 healthy controls who underwent standard laboratory tests, colonoscopy, serum C4, FGF19 and fecal calprotectin (FC). Patients were split into six groups: 30 patients with active IBD, 21 patients with IBD in remission reporting a high number of bowel movements per day, 21 patients with IBD after surgery (ileal resection), 23 patients with IBS-D, 14 patients with MC and 11 healthy subjects (controls).

We compared serum C4 concentrations, measured by high-resolution mass spectrometry (HRMS) quantitative analysis with FGF19 using ELISA, between the groups. From the area under the receiver operating characteristic curve (AUROC) we identify the optimal cut-off C4 concentrations for the diagnosis of diarrhea attributable to BAM.

Results: Based on cut-off levels of FGF-19 (< 60 pg/mL) and bowel movements, the diagnosis of BAM was confirmed in n=69/109 patients (63.3%) and excluded in n=40 (36.7%) compare to healthy controls. Median levels of C4 in patients with IBD active were 53.1 ng/mL, IBD remission was 52.2 ng/mL, IBD after surgery was 85.7 ng/mL, IBS-D were 7.5 ng/mL, MC was 69.3 ng/mL and healthy controls were 3.7 ng/mL. IBD patients in remission (FC < 100 μ g/g) with up to 4 bowel movements daily was n=16 (76.2%) and concentration of C4 above 48.9 ng/mL were found in n=13 (61%) of the patients.

When we analyzed only patients with diarrhea and those identified with FGF-19 (< 60 pg/mL), we estimate a C4 cut-off of 48.9 ng/mL with 82.6% sensitivity and 84.3 % specificity (AUROC, 0.89) in all the patients with chronic diarrhea.

Above this cut-off, 68% of patients had a serum concentration of FGF19 < 60 pg/mL compared to 14% below this threshold (P < .001). C4 concentrations correlated with the stool frequency per day/bowel movements (r = 0.709; P < .001) and correlated inversely with FGF-19 concentrations (r = -0.741; P < .001).

Conclusion: These findings indicate that, in chronic diarrhea patients, BAM is a common and very under-diagnosed condition. Serum C4 and FGF-19 could be used for screening biomarkers for BAM in patients with IBD and MC. C4 above 48.9 ng/mL and FGF-19 below 60 pg/mL identify patients with diarrhea likely attributable to BAM with high diagnostic accuracy and IBD patients in remission with found bile acid diarrhea can benefit from additional treatment with bile acid binders.

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P0282

BILE ACID DIARRHOEA: A COMMONLY OVERLOOKED CONDITION WITH DELAYED DIAGNOSIS

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Introduction: Diarrhoea is a common indication for referral to the gastroenterology clinic with a wide differential diagnoses, including bile salt malabsorption (BAM). The aim of our study was to review the use of SeHCAT scan as part of investigation of chronic diarrhoea and see if there is a delay in diagnosing BAM in patients with chronic unexplained diarrhoea.

Aims & Methods: 200 patients were randomly selected from a group of 550 patients who had undergone a SeHCAT scan in a two-year period, November 2017 to October 2019. We used our hospital electronic patient records to collect data on patient demographics, average time from initial gastroenterology referral to SeHCAT scan date, and whether they had had prior GI investigations.

Results: There were 200 patients included in this study (females 136, males 64, median age 52.5, range 19-88 yrs). 116 patients (58%) had a negative SeHCAT scan. There were 84 (42%) positive SeHCAT scans confirming BAM of which 24 (28.5%), 13 (15.4%), 26 (31%), and 21 (25%) were classified as mild, moderate, severe and borderline, respectively. 176 patients (88%) had prior GI investigations before undergoing SeHCAT scan. The average time from initial referral to SeHCAT scan was 9.7 months (range 1-52 months).

Conclusion: Our study shows that BAM is a common cause of diarrhoea (42% in our cohort), but there seems to be a significant delay in diagnosis, which may lead to patient suffering and potentially further unnecessary tests. We suggest that BAM to be considered early in the diagnostic work-up of patients with chronic diarrhoea.

Disclosure: Nothing to disclose

P0283

BILE ACID DIARRHOEA OUTSIDE TERTIARY CENTRES-HOW BAD IS BAD?

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Introduction: Chronic diarrhoea causes significant morbidity. Bile acid diarrhoea (BAD) is considered causal in up to 1/3 of people investigated for IBS-D. BSG guidelines recommend investigation for BAD using SeHCAT scanning / serum bile acid precursors.^[1] Empirical trial of treatment is not recommended. Access to tests can be limited in district general hospitals (DGH). We report our experience in a DGH where diagnostic testing is provided 60 km away.

Aims & Methods: Our aim was to review our investigation of chronic diarrhoea in particular when suspecting BAD. A retrospective notes review was performed for all outpatients from East and North Herts NHS trust (catchment population 600,000) who had SeHCAT scans performed by a

regional service (Mount Vernon Hospital) in 2019. Data were collected on demographics, symptoms, risk factors, other investigations, time between first clinic and scanning and prior empirical treatment. Comparison were made between positive and negative groups using multiple regression analysis.

Results: 50 scans were requested of which 48 results were available. Median age was 49 (23 - 84y), 33(69%) female. 21 scans (44%) were positive for BAD, 3 (14%) mild, 10 (48%) moderate, 8 (38%) severe. 3 patients with incomplete data were excluded from subsequent analyses, leaving 45 scans for further analysis (19 positive, 26 negative). Risk factors are presented in Table 1. A statistically significant association between cholecystectomy and positive SeHCAT scan was found ($p=0.026$). There was considerable delay in diagnostic confirmation for some patients with a positive test taking 1 month to 10 years. Overall 41/45 (91%) patients had prior testing with faecal calprotectin, 32/45 (71%) patients had colonoscopies of whom 24 (75%) had colonic biopsies, 43/45 (96%) had thyroid function checked and 39/45 (87%) were screened for coeliac disease. 10 patients had empirical treatment with bile acid sequestrants before scanning, only 3 of whom later had positive scans.

Risk factors	Negative SeHCAT scan (26)	Positive SeHCAT scan (19)
Cholecystectomy	5 (19%)	10 (53%)
Crohn's	1 (4%)	1 (5%)
Right hemicolectomy	1 (4%)	1 (5%)
Coeliac	2 (8%)	0 (0%)
Diabetes	2 (8%)	2 (10%)
Other surgery	1 (4%)	0 (0%)
No risk factors	16 (59%)	7 (37%)

[Figure 1: Risk factors for BAD in chronic diarrhoea]

Conclusion: Our study has shown a burden of incident BAD in the outpatient DGH setting. This is underestimated due to use of empirical treatment without testing, lack of investigation of some patients with disease and referral for SeHCAT scanning in other centres not identified. Patients had appropriate initial investigations performed for chronic diarrhoea. In keeping with larger studies from tertiary centres prior cholecystectomy is the commonest predisposing factor (type III) and >1/3 of patients had no identified risk factor (type II). There are limited data regarding BAD investigation and management in DGH setting where patients have to travel considerable distance for testing. There are problems associated with empirical treatment including current drug availability in the UK. National management guidelines based on large studies and wider availability of economically viable testing are needed.

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Disclosure: Nothing to disclose

P0284

CLINICOPATHOLOGICAL FEATURES AND GENOMIC CHARACTERISTICS OF PRIMARY SMALL-BOWEL CANCER IN JAPANESE POPULATION

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Introduction: Current understanding of clinicopathological features and genomic alterations of small-bowel cancer is limited due to its rarity. We aimed to identify its clinicopathological features, genomic alterations associated with prognosis and recurrence.

Aims & Methods: We retrospectively examined 24 patients [mean age ($\pm$ SD): 61.7 $\pm$ 11.7 years, and the frequency of males: 75% (16/24)] with 29 primary small-bowel cancer treated by surgery between May 2005 and August 2018. First, we evaluated the mismatch repair status using immunohistochemical (IHC) staining for MLH1, MSH2, MSH6, and PMS2 proteins. Next, we extracted DNA from 29 lesions, and underwent targeted genomic sequencing analyzing using a panel of 90 cancer-related genes. We compared each cancerous tissue with the counterpart normal tissue and normal mucosa to detect mutations. Finally, we assessed the association between the clinicopathological features, treatment outcomes, prognosis, and genomic alterations.

Results: 92% of the patients (22/24) exhibited disease symptoms. The lesions in 83% (24/29) were located in the jejunum. Mean tumor diameter ($\pm$ SD) was 42.2 $\pm$ 18.4 mm. The rate of histopathological findings for tub1/2, pap, por, muc, and sig were 76% (22/29), 7% (2/29), 7% (2/29), and 3% (1/29), respectively. The rate of Type 1, Type 2, and Type 3 tumor morphologies were 10% (3/29), 59% (17/29), and 28% (8/29), respectively. The rate of pathological stage I, II, III, and IV (according to the Japanese Classification of Colorectal Carcinoma) were 3% (1/29), 31% (9/29), 34% (10/29), and 31% (9/29), respectively. Around 66% (16/24) of patients could undergo R0 resection. IHC staining revealed that 55% (16/29) exhibited deficient mismatch repair (dMMR) (MLH1 and PMS2 absent in 10 lesions, MSH2 and MSH6 absent in 3 lesions, and only MSH6 absent in 3 lesions). There were no differences between patients with dMMR and proficient MMR in terms of overall survival (OS) and disease specific survival (DSS), as revealed by Kaplan-Meier analysis. Examination of 27 lesions in 23 patients revealed that the most common genomic alterations of small-bowel cancers were TP53(48% [13/27]), followed by KRAS(44% [12/27]), ARID1A(22% [9/27]), PIK3CA(26% [7/27]), APC(26% [7/27]), SMAD4, NOTCH1 NOTCH3, CREBBP, PTCH1, and EP300(22% [6/27]). Median value of the tumor mutational burden (TMB) was 14 mutations/Mb. In the lesions with TMB $\geq$ 10 mutations/Mb (n = 18), the frequency of dMMR was 56% (10/18). There was no difference between genomic alteration in each gene. The OS and DSS of patients with TMB < 10 mutations/Mb (n=6) was related significantly to the poorer prognosis of such patients than the patients with TMB $\geq$ 10 mutations/Mb (n=17) ($P < 0.05$).

Moreover, in the patients with TMB $\geq$ 10 mutations/Mb, the frequency of the depressed type (100% [18/18]) was significantly higher than in patients with TMB < 10 mutations/Mb ($P=0.03$). On the other hand, 16 patients could be treated via R0 resection. Of them, the patients with mutant SMAD4 had poorer recurrence free survival than those with wild-type SMAD4($P < 0.05$).

Conclusion: Most of the patients with primary small-bowel cancer were diagnosed at an advanced stage and had poor prognosis. TMB levels correlated with tumor prognosis and macroscopic characteristics of the tumor. *SMAD4* mutation was associated with recurrence after R0 resection.
Disclosure: Nothing to disclose

P0285

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF MALIGNANT SMALL BOWEL NEOPLASIAS: PROGNOSIS OF A SILENT ENTITY

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Introduction: Small bowel tumors are rare entities with an uncertain prognosis which are difficult to diagnose. Until today, there are only a few studies evaluating the predisposing factors, histology, and prognosis of these patients.

Our aim was to analyze the clinical characteristics of the patients diagnosed with small bowel malignant neoplasias in our hospital.

Aims & Methods: We performed a retrospective analysis in our cohort of patients with small bowel tumor who were diagnosed in our center between January 1st 1989 and December 31st 2019. Demographic, clinical and therapeutic characteristics were collected. Patients diagnosed with lymphoma were excluded due to their different staging and treatment.

Results: 85 patients diagnosed with solid bowel cancer were identified. The average age of diagnosis was 67.42 years (SD 15.75) and there were more men than women (61.18%, n = 52). The main symptom at diagnosis was abdominal pain in 38.82% cases, gastrointestinal bleeding in 26.18% and bowel obstruction in 21.43% of the patients. Only 8.24% (n = 7) of the subjects had some risk factor associated to bowel tumor (Crohn's disease, Lynch syndrome or Familial Adenomatous Polyposis-FAP).

The most frequent was duodenal location (64.71%), followed by ileum (20%) and jejunum (15.29%). A percentage of 16.47% were duodenal papilla tumors. Regarding the diagnosis, 52.94% tumors were accessible by endoscopic study. The CT scan made a (was contributory to the diagnosis) diagnostic contribution in 75.29% patients while 22.35% were diagnosed during the surgery. 51.19% of the patients needed more than (a) one test to establish the diagnosis.

The most frequent tumor was adenocarcinoma (63.53%), followed by GIST (9.30%), no differentiate carcinoma (7.06%) and neuroendocrine tumor (5.81%). 87.3% patients were diagnosed in an advanced stage of the disease (T4 in 29.41.66% cases, T3 in 18.82% and 44.7 were not staged due to poor prognosis). In the extension study, 58.82% had metastases at the point of the diagnosis.

Regarding the therapeutic approach, 34.19% of the patients received chemotherapy as an initial treatment (meanwhile) while surgical intervention was required in 65% of the patients attending to diverse indications. The median survival time was 15.08 months (SD 51.26). However, 26.19% of the patients reached clinical remission, 45.24% clinical progression and relapse in 10.71%.

Conclusion:

1. Malignant neoplasms of the small intestine are rare and difficult to diagnose due to their silent nature. Many of them are not detected until surgery is required because of some other complications.
2. The diagnosis of these tumors often occurs in advanced stages associating a poor prognosis.

3. It is important to diagnose at an early stage in order to increase the survival rate of these patients.

Disclosure: Nothing to disclose

P0286

DOES URGENT BALLOON ASSISTED ENTEROSCOPY IMPACTS REBLEEDING AND MORTALITY IN OVERT OBSCURE GASTROINTESTINAL BLEEDING?

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Introduction: The diagnostic yield (DY) and therapeutic yield (TY) of balloon-assisted enteroscopy (BAE) in overt obscure gastrointestinal bleeding (OGIB) is higher in the first 72h.

Aims & Methods: This study aimed to evaluate if this higher DY and TY after urgent BAE impacted the rebleeding rate, time to rebleed and mortality. Retrospective cohort-study, which consecutively included all patients submitted to BAE for overt OGIB, between 2010-2019. Patients were distributed in 2 groups:

- (1) Urgent BAE;
- (2) Non-urgent BAE.

Rebleeding was defined as an Hb drop >2 g/dL, need for transfusional support or presence of melena/hematochezia.

Results: Fifty four patients were included, of which 17 (31.5%) were submitted to BAE in the first 72h. DY and TY of urgent BAE (DY 88.2%; n=15; TY 94.1%; n=16) was higher compared to non-urgent BAE (DY 59.5%; n=22; TY 45.9%; n=17) (DY p=0.03) (TY p=0.001).

The rebleeding rate at 1, 2, and 5 years was 32.0%, 34.0% and 37.0%, respectively. Rebleeding was lower after urgent BAE (17.6%; n=3) compared to non-urgent BAE (45.9%; n=17) (p=0.04). Rebleeding tended to occur earlier in non-urgent BAE, being at 6-months (32.5%) and 36 months (41.3%) (p=0.05). OGIB related mortality was 8.1% (n=3) for non-urgent BAE and 0% for urgent BAE (p=0.5).

Conclusion: Urgent BAE is associated with higher DY and TY with lower rebleeding and trend toward higher rebleeding-free time.

Disclosure: Nothing to disclose

P0287

PREDICTING THE RISK OF REBLEEDING AFTER CAPSULE ENDOSCOPY IN OBSCURE GASTROINTESTINAL BLEEDING - EXTERNAL VALIDATION OF THE RHEMITT SCORE

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Introduction: Prediction of rebleeding after small bowel capsule endoscopy (SBCE) in obscure gastrointestinal bleeding (OGIB) is challenging. The recently described RHEMITT score includes 7 variables: chronic kidney disease (CKD); heart failure (HF); P1/P2 lesions (Saurin's classification); major bleeding; incomplete examination; smoking and endoscopic treatment.

This tool has been shown to accurately predict the risk of recurrence after a SBCE study.

Aims & Methods: The primary aim of this study was to perform an external validation of the RHEMITT score.

Retrospective cohort-study, which consecutively included all patients submitted to SBCE (*Mirocam*®) for OGIB between January 2017 and December 2018. Rebleeding was defined as: (1) a drop in hemoglobin >2g/dL or (2) Melena or hematochezia. The RHEMITT score was calculated and subsequently the accuracy of the score for the prediction of rebleeding was assessed.

Results: One-hundred and sixty patients were enrolled. Mean age was 65.8±13.6 years and 58.1% (n=93) were female. The mean follow-up time was 20 (SD 9) months. Rebleeding occurred in 14.4% (n=23). Rebleeding at 6, 12, 18 and 24 months was 6.3%, 12.0%, 14.2% and 15.5% respectively. There was a significant association between the RHEMITT score and rebleeding ($p < 0.001$). The area under the (AUC) ROC curve was 0.756 ($p < 0.001$). Rebleeding occurred earlier in intermediate and high-risk patients (RHEMITT score >3) being at 6-months 13.6% and 24 months 28.4% ($p < 0.01$).

Conclusion: The present study carried out in an external validation cohort confirms the usefulness and accuracy of the RHEMITT score in predicting rebleeding after SBCE.

Disclosure: Nothing to disclose

P0288

HEMOPILL ACUTE®: PRELIMINARY RESULTS USING A SENSOR BASED TELEMETRIC CAPSULE SYSTEM IN PATIENTS WITH EGD NEGATIVE ACUTE MID GI BLEEDING

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Introduction: 2-5 % of all GI bleedings occur in the small intestine and are often a clinical challenge. We report on first experiences with the HemoPill acute® (HPa) capsule (Ovesco Corp., Tuebingen, Germany). The sensor based low-cost capsule has been approved and CE certified for the detection of acute bleedings in the upper GI tract in 2019. The capsule contains a photometric sensor and determines the intensity ratio of violet and red light calculating the so-called HemoPill indicator (HI). The measurement had been unaffected by food components in prior tests performed by the Schmidt A., et al. as base for certification of the product. The capsule is connected via Bluetooth to a mobile HPa receiver with instant visualization of the findings. Interpretation: Fresh blood/hematin - HI 1.0-1.5; other contents of the digestive tract including bilirubin - HI 0.50-0.9.

Aims & Methods: From August 2019 - April 2020, the HPa was used in 13 patients with acute GI bleeding and negative EGD in an observational trial (8 men, 5 women, age 28 to 84 years, Glasgow-Blatchford score 6 to 12 (M 10; SD 2). A double balloon enteroscopy (DBE) followed in case of HI ≥ 1.0 for detection of a small intestinal bleeding source.

Results: The application of the HPa was associated to no complications in all 13 patients. In 9 cases the capsule was administered orally and in 4 cases by endoscopic placement to the duodenum. The procedure was technically successful all 13 cases. Albeit in one case the measurement was interrupted intermediately due to the HP Receiver being out of range, the incomplete measurement non the less showed a HI ≥ 1.0 . A total of 7 / 13 HPa exams were positive with an HI ≥ 1.0 (m 1.4; 1.1-1.8) indicating the detection of blood in the small intestine by the capsule. Double balloon enteroscopy followed within 24h (median 22 h) and confirmed in 3/7 cases active bleeding. In all 7 cases angiodysplasia was detected as probable bleeding source by DBE and Ar+ plasma coagulation was performed in all 7. All other cases received standard elective evaluation of the colon

± small intestine. None of them rebled. In 1/6 cases a jejunal ulcer was detected without active bleeding at the time of evaluation by video capsule endoscopy.

Conclusion: In this preliminary observational trial HemoPill acute® rapidly and reliably detected active small intestinal bleeding in a group of 13 patients with emergency admission due to suspected acute GI bleeding and negative EGD. A further prospective comparative evaluation is to be awaited to better classify the value of this promising new system.

References: Schmidt, A., Zimmermann, M., Bauder, M., Kuellmer, A. & Caca, K. Novel telemetric sensor capsule for EGD urgency triage: a feasibility study. *Endosc. Int. Open* 07, (2019).

Disclosure: The HemoPill acute® system was granted free of charge by Ovesco Corp., Tuebingen, Germany

P0289

GASTROINTESTINAL FIBROSIS AND MICROVASCULAR ABNORMALITIES ARE KEY HISTOPATHOLOGICAL FEATURES IN GENETICALLY-DRIVEN, MITOCHONDRIAL-TYPE INTESTINAL PSEUDO-OBSTRUCTION

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Introduction: Severe gastrointestinal (GI) dysmotility, e.g. chronic intestinal pseudo-obstruction, is commonly detected in mitochondrial disorders of genetic origin, including mitochondrial neurogastrointestinal encephalomyopathy (MNGIE). This is an extremely rare disease caused by *TYMP* mutations responsible for thymidine phosphorylase (TP) enzyme defect, nucleoside accumulation and toxic effects in the brain, skeletal muscle and GI tract along with mtDNA damage. MNGIE is a devastating and fatal disease with a clinical picture dominated by GI dysmotility and neuro-muscular impairment. Recent therapeutic strategies, aimed at replacing permanently TP via bone marrow or liver transplant, lead to a stably recover of the biochemical imbalance, without affecting pathological alterations of the GI tract (e.g. smooth muscle degeneration) and the severe complications (massive GI bleeding). Based on consistent evidence indicating that TP exhibits significant angiogenic properties, we hypothesize that microvascular abnormalities and related hypoxic changes occur in the GI tract of MNGIE pts.

Aims & Methods: The aim of our research was to provide an accurate morphometric analysis of the enteric microvasculature in the jejunum submucosal layer of MNGIE pts and a quantitative assessment of fibrosis and neuronal damage as possible index of hypoxia-induced tissue damage. Jejunal surgical specimens biopsies were collected from 5 MNGIE (4M; 20-38 yrs) pts and 9 pts undergoing resection due to non-complicated GI tumors who served as controls (CTR; 5 M; 47-71 yrs). Formalin fixed-paraffin embedded tissue sections were stained with orcein to measure and count blood vessels subdivided in 4 classes: >300µm in diameter (large); 300-101µm (medium); 100-50µm (small) and < 50µm (very small). Sections were stained with Sirius Red/Fast Green collagen assay to determine vascular fibrosis and immunolabeled with neuron-specific enolase (NSE) to count submucosal and myenteric neurons per ganglion and inter-myenteric ganglion distance. The thickness of the longitudinal muscle layer was also determined.

Results: Compared to CTR, MNGIE pts showed a decreased area of vascular tissue ($P=0.002$) and a two-fold increase of submucosal vessels/ mm^2 ($P=0.019$). These findings were associated with a change of the microvascular pattern characterized by an increased number of small size ($P=0.001$) and a decrease in medium ($P=0.0010$) and large size ($P=0.0163$) vessels. The jejunal fibrosis index increased 1.7 fold in MNGIE pts vs. CTR ($P=0.0043$). MNGIE exhibited a reduced thickness of the longitudinal muscle layer ($P=0.0033$), an increased distance between adjacent ganglia ($P=0.001$) and a reduction of the myenteric, but not submucosal, neuron number ($P=0.001$) vs. CTR.

Conclusion: Alterations of the vasculature together with smooth muscle fibrosis and enteric neuronal loss are histopathological features of MNGIE. GI vasculature abnormalities in MNGIE may affect the enteric neuro-muscular layer integrity due to hypoxia.

Disclosure: Nothing to disclose

P0290

SOMATOSTATIN ANALOGUES ARE EFFECTIVE AND SAFE IN TRANSFUSION-DEPENDENT GASTROINTESTINAL BLEEDING DUE TO ANGIODYSPLASIA: AN INDIVIDUAL PATIENT DATA META-ANALYSIS

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Introduction: Several small cohort studies and one randomised controlled trial suggest that somatostatin analogues (SSA) may decrease re-bleeding rates in patients with gastrointestinal angiodysplasia. The true effect size of SSA treatment on clinical outcomes in bleeding angiodysplasia is unknown.

Aims & Methods: The aim of this individual patient data meta-analysis was to establish the efficacy of SSA treatment on blood transfusion need of patients with gastrointestinal angiodysplasia. We performed a systematic search up to February 2020 using MEDLINE, EMBASE and the Cochrane Library to identify articles on SSA effect on angiodysplasia. The primary outcome was the mean absolute and percentage decrease in red blood cell transfusion during SSA treatment. We used multilevel Poisson regression to account for differences in study durations. We categorised patients according to percentage decrease in red blood cell transfusion. Patients

were classified as good responders ($\geq 50\%$ reduction) or poor responders ($< 50\%$). Mean absolute and percentage increase in haemoglobin level and adverse events were considered as secondary outcomes.

Results: We identified 12 studies and obtained individual patient data from 9 cohorts. Aggregated data were available for another 2 studies. We analysed data from 212 patients from 11 studies (mean age 71 years, 53% men).

Patients experienced a mean absolute decrease in red blood cell transfusion from 13.17 to 3.53 in a mean period of 12.2 months (Incidence rate ratio [IRR], 0.27; 95% CI, 0.25-0.29). The mean percentage decrease in RBC transfusion was 73.2% (95% CI 70.9%-75.4%; $p < 0.0001$). A good response was seen in 177/212 patients (83.5%), and 35/212 patients (16.5%) had a poor response. Most good responders (109/177 patients; 61.6%) did not need a red blood cell transfusion while on SSA treatment.

The mean absolute haemoglobin level increased from 7.08 to 9.64 g/dl during SSA treatment (IRR, 1.36; 95% CI, 1.24-1.50; percentage increase 36.2% (95% CI 23.8%-49.8%; $p < 0.0001$)).

Adverse events occurred in 38/212 patients (17.9%) (IRR, 1.09; 95% CI 14.8%-25.7%). Common adverse gastrointestinal events were loose stools (3.3%), cholelithiasis (2.4%), flatulence (1.9%) and abdominal pain (1.4%). Other common adverse events were local pain or mild erythema at the injection site (3.8%) and impaired glucose tolerance (1.4%). Only 10/212 patients (4.7%) discontinued SSA due to adverse events (IRR, 1.31; 95% CI 4.6%-8.3%).

Conclusion: SSA treatment is effective and safe in the majority of patients with transfusion-dependent bleeding secondary to gastrointestinal angiodysplasia.

Disclosure: Nothing to disclose

P0291 WITHDRAWN

Poster presentations

Nutrition

Poster Presentations Nutrition

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Nutrition

09:00-19:00 / Poster Exhibition

P0292 WITHDRAWN

P0293

DETERMINANT COMPONENTS OF METABOLIC SYNDROME REGRESSION AND PROGRESSION: A POPULATION-BASED COHORT

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Introduction: Metabolic syndrome (MetS) as a non-communicable disease (NCD) had become epidemic in many countries of the world. MetS risk factors were investigated in different studies. However, assessed factors affect the progression and regression of the MetS have not been reported in any longitudinal study.

Aims & Methods: This study aimed to determine the risk factors related to regression and progression of metabolic syndrome, in a 4-year cohort study. This cohort study was carried out in Shiraz, Iran which lasted up to 2018. Participants (≥ 18 years old) were randomly selected via a multistage proportional and cluster random sampling. A total of 540 individuals participated in both phase of the study. Participants were categorized into 3 categories of regressed, progressed and unchanged metabolic syndrome (MetS). Demographic, anthropometric and biochemical parameters were assessed for each individual in both phase. For quantitative variables, differences (phase 2-phase 1, delta: Δ) between the two phase of study were calculated. Variables with P value less than 0.2 in univariable analysis, were entered into the multi-nominal logistic regression analysis to examine the odds of regression and progression of MetS, while un-changed group was considered as baseline category. Receiver Operating Characteristic (ROC) analysis was done for significant variable (p<0.10).

Results: Based on IDF, MetS had been regressed and progressed in 42 participants (7.7%) and 112 (20.7%) participants respectively, in the second phase. These amounts were 42 (7.7%) and 117 (21.6%) respectively based on ATP III. Results of multiple variable analysis revealed that increased age, positive Δ-TG, and Δ-FBS, significantly increased the odds of MetS progression based on IDF and ATP III definitions, while negative Δ-HDL and Δ-neutrophil to lymph ratio increased the odds of progression. On the other hand, negative Δ-TG and positive Δ-HDL significantly increased the odds of MetS regression based of both IDF and ATP III. Other variables did not affect regression and progression of the disease significantly.

Conclusion: Management of hypertriglyceridemia, hyperglycemia, and HDL is a critical, non-invasive and accessible approach to change the trend of MetS.

Disclosure: Nothing to disclose

P0294 WITHDRAWN

P0295

SPATZ 3 ADJUSTABLE BALLOON SYSTEM: EFFICACY AND SAFETY ISSUES OF A DUAL CENTER EXPERIENCE

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Introduction: Intra-gastric balloons for weight loss and as bridge to major bariatric surgery are effective tools, but they could be associated with early period intolerance and a diminished effect within 8-12 weeks. The introduction of an adjustable balloon could improve comfort and offer greater efficacy over the time. Spatz 3™ is a dynamic bariatric device with a long implantation time (12 months), system for inflation and deflation of the balloon, and safety mechanism that precludes its bowel migration despite an eventual deflation. This is a new improved version of Spatz adjustable balloon system and there are few data about its efficacy and safety in a large followed up bariatric population.

Aims & Methods: The aim of our study was to assess Spatz3 efficacy in terms of weight loss and maintenance of weight after removal and its long term safety issues. Implantations of Spatz 3 in 138 patients were reviewed and data about demographics, weight loss, bridging to surgery, early and late complications and weight maintenance were collected from the prospectively collected database of two tertiary Endoscopic centers. Mean age of the study population was 47.8 years and its mean starting BMI was 40.2. A 12 months treatment was scheduled and volume adjustment was proposed in case of patient intolerance or weight loss plateau.

Results: From January 2016 to April 2019, 138 obese patients (pts) were treated with Spatz 3 balloon endoscopic implantation and among these 71 pts used the treatment as bridge to major surgery. The mean weight loss above a 12 months period was 24.8 kilograms. In 8 pts the device was removed after 3 weeks for intolerance. Down volume adjustment was performed in 9 pts (mean volume 180 ml) allowing them to continue the therapy, volume balloon increase was instead performed in 19 pts (mean time : 5.8 months, mean volume 235 ml) yielding an additional mean weight loss of 4.8 kilograms. No Spatz rupture, gastric perforations or major clinic complications occurred: only small esophageal and gastric erosions that did not required balloon extraction.

Conclusion: Even if with a retrospective analysis, Spatz 3 balloon seems to be an effective and safe device to treat obesity with a mean weight loss of 24 kilograms in the study population within a 12 months period with no early or late complication. The possibility to adjust the balloon volume can reduce intolerance and improve weight loss when a plateau is reached.

Disclosure: Nothing to disclose

P0296

ROLE OF OMEGA-3 FATTY ACIDS AND PROBIOTICS IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN RATS

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Introduction: Liver is the most complicated and major internal organ in the human body. It plays an essential role in the preservation of systemic lipid homeostasis through its multiple and diverse functions. Nonalcoholic fatty liver disease (NAFLD) is the most public chronic liver disease universal, both in adults and in children. NAFLD characterizes a spectrum of liver diseases that range from hepatic steatosis to steatohepatitis and cirrhosis. NAFLD is more predominant in overweight and obese people. Omega-3 fatty acids are not manufactured by the body and must be obtained through foods or supplementation so they are essential fatty acids. Probiotics is living microorganisms that, when managed in adequate amounts, talk a health benefit on the host. Many statistics from animal experiments have showed that modulating gut microbiota with probiotics preparations has a beneficial effect on NAFLD.

Aims & Methods: The aim of the current study is to evaluate the effect of omega 3 fatty acids and probiotics against special diet induced Nonalcoholic Fatty Liver Disease (NAFLD).

Study design and methods: Fifty adult albino rats were classified into five groups(10 rats each).

Group 1: Negative control group.

Group 2: positive control group rats fed on choline methionine deficient diet and 20% fructose in the drinking water for 8weeks and 3 treated groups.

Group 3: diseased rats fed on choline methionine deficient diet treated with flaxseeds oil 1.7ml/kg bw orally.

Group 4: diseased rats fed on choline methionine deficient diet treated with mixture live probiotics strain140 mg/kg powder in diet. And;

Group 5: diseased rats fed on choline methionine deficient diet treated with mix flaxseeds oil 1.7ml/kg bw orally and live probiotics strain 140 mg/kg orally.

Results: Treatment of mixed flaxseeds oil 1.7ml/kg bw orally and live probiotics strain 140 mg/kg powder in diet significantly improved serum blood lipid,serum liver enzyme(AST,ALT), transforming growth factor beta(TGFB), tumor necrosis factor (TNFα),oxidative stress levels, interleukin-6 (IL-6) and both hepatocytes' fats and the portal tracts inflammation than the other treated groups in comparison to the control positive group. On the other hand, Malondialdehyde (MDA) level was significantly decreased in the group treated by mixed flaxseeds oil 1.7ml/kg bw orally and live probiotics strain 140 mg/kg powder in diet than the other treated groups in relation to the control positive group.

Conclusion: These results suggest that there are beneficial effects of the treatment of rats with NAFLD by combination of probiotics and omega-3 fatty acids for 8 weeks, as they reduce liver fat, improve serum lipids, metabolic profile and inflammatory state.

Disclosure: Nothing to disclose

P0297

WEIGHT AND METABOLIC OUTCOMES ASSOCIATED WITH ENDOSCOPIC SLEEVE GASTROPLASTY: A MULTICENTER STUDY

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Introduction: Endoscopic Sleeve Gastroplasty (ESG) is an incisionless, minimally invasive remodeling of the greater curvature of the stomach to achieve weight loss in patients with obesity. Multiple studies have demonstrated significant reduction in Total Body Weight Loss (TBWL) with minimal adverse effects. However, a paucity of data exists regarding metabolic outcomes associated with ESG. We aim to identify 3-month metabolic outcomes in an international multicenter cohort of obese patients who underwent ESG.

Aims & Methods: This is a retrospective multicenter international study of consecutive patients across four centers who underwent ESG between June 2016 and September 2019. Electronic medical records were used to collect baseline data. Primary outcome was metabolic outcomes, as defined by mean systolic and diastolic blood pressure, liver enzymes, lipid profile, BMI, weight, and A1C. Secondary outcome was medication requirements for comorbidities. Data was collected pre-ESG and at an average of 2.4 month follow up.

Results: A total of 92 patients included, mean age of 43.2 years (SD 11.4) and BMI 39.9 kg/m (SD 8.1). Baseline labs and anthropometric data pre-op and at 3 months follow up are shown in Table 1. At 2.4 months, there was a significant reduction of systolic blood pressure by 11mmHg (p <0.00003), diastolic blood pressure by 4.65 (p <0.004), weight by 24.4 lbs (p <0.00001), BMI by 4.1 kg/m (p <0.00001), and ALT by 8.62 units (p < 0.004) (see Table 2). For secondary outcomes, 23/67 diabetic patients reported they were able to reduce or stop insulin, 10/66 (15%) GERD patients reported stopping proton-pump inhibitors, and 24/68 (35%) hypertensive patients reported stopping or reducing hypertensive medications.

Conclusion: Endoscopic Sleeve Gastroplasty resulted in improved blood pressure, liver injury, and significant weight loss at 3-month follow-up. Additionally, patients reported a significant reduction in insulin, anti-hypertensive, and GERD medications. ESG has a prominent role in weight loss but also a significant impact on metabolic diseases.

Disclosure: Michel Kahaleh is a consultant for Apollo Endosurgery

P0298 WITHDRAWN

P0299

GASTRIC SLEEVE SURGERY WITH DUODENAL SWITCH HAS MINOR EFFECTS ON GASTRIC EMPTYING AND INTESTINAL TRANSIT TIMES, LUMINAL PRESSURES AND MOTILITY INDICES AS EVALUATED WITH WIRELESS MOTILITY CAPSULE (SMARTPILL)

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Introduction: Sleeve gastrectomy is used to induce weight reduction in obesity. Functional gastrointestinal (GI) disorder symptoms are reported in obese patients. The impact of the procedure on GI tract transit and pressures has not been reported.

Aims & Methods: Obese subjects scheduled for a gastric sleeve were recruited wireless motility capsule (WMC) testing before and one year after sleeve gastrectomy. Gastrointestinal luminal pressures and transit results were compared to WMC results in normal subjects reported by Wang. Ethics approval by Uppsala Ethics Board 2012/142.

Results: Sixteen obese subjects (pre-surgery BMI 54.7±2.1; 7 females) underwent WMC procedure prior to a sleeve gastrectomy and a second WMC approximately one year after the procedure (post-surgery BMI 33.6±2.1). Regional transits were not significantly different pre and post sleeve and were comparable to normal subjects. The average gastric emptying time by WMC pre and post sleeve was within the normal range (1:45hr-5hr). No subjects showed gastric delay prior to sleeve gastrectomy and one subject was delayed post procedure. Two subjects displayed rapid gastric emptying pre-procedure and 4 subjects post procedure. Prevalence of SBTT delay (19%) was the same prior to and post procedure while 5 subjects had rapid SBTT post procedure compared to 1 subject before procedure. Average maximum gastric and antral pressures increased post sleeve gastrectomy but not significantly. Small bowel and duodenal average maximum pressures declined significantly post procedure. Motility index and sum of the amplitudes were not significantly different in any region.

Conclusion: Rapid gastric emptying was observed in 25% of patients one year after sleeve gastrectomy. Prevalence of subjects with abnormal transits increased 42% post procedure. (7 vs 12) The maximum pressure contractions observed in the antrum and stomach increased but not significantly while duodenum and small bowel pressures decline significantly post sleeve gastrectomy.

Disclosure: Nothing to disclose

P0300

TRANSVERSUS ABDOMINIS PLANE BLOCK IS EFFECTIVE AND SAFE A PART OF MULTIMODAL ANALGESIA IN BARIATRIC SURGERY: A META-ANALYSIS AND SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Pain after bariatric surgery can prolong recovery. This patient group is highly susceptible to opioid-related side effects. Enhanced Recovery After Surgery guidelines strongly recommend the administration of multimodal medications accompanied by local anesthetic infiltration to reduce narcotic consumption.

Aims & Methods: However, the role of transversus abdominis plane block (TAP block) in multimodal analgesia of weight loss surgeries remains controversial. Our study is reported using Preferred Reporting Items for Systematic Reviews and Meta-analyses. A systematic search was performed in four databases for studies published up to September 2019. We considered randomized controlled trials that assessed the efficacy of perioperative ultrasound-guided (USG) TAP block as a part of multimodal analgesia in patients with laparoscopic bariatric surgery.

Results: Eight studies (525 patients) were included in the meta-analysis. Pooled analysis showed lower pain scores with USG-TAP block at every evaluated time point, and lower opioid requirement in the USG-TAP block group [weighted mean difference (WMD)=-7.59 mg, 95% CI (-9.86; -5.39), p<0.001]. Significant risk reduction for nausea and vomiting were also observed with USG-TAP block [RR=0.24, 95% CI (0.11-0.55), p<0.001]. Time to ambulate was shorter with USG-TAP block [WMD = -2.22 hours, 95% CI (-3.89; -0.56), p=0.009]. This intervention also seemed to be safe: only three non-severe complications with USG-TAP block were reported in the included studies.

Conclusion: Our results support the incorporation of USG-TAP block into multimodal analgesia regimens of ERAS protocols for bariatric surgery. However, high heterogeneity across studies and the risk of bias in included studies render the need for further research in this field.

Disclosure: Nothing to disclose

P0301

ASSESSMENT OF BILE ACIDS FRACTIONS IN BILE IN CHILDREN WITH OVERWEIGHT AND OBESITY AND BILIARY DYSFUNCTION

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Introduction: Biliary dysfunction having an impact on the bile acid composition in children with overweight and obesity can lead to the progression of structural changes in the liver.

Aims & Methods: To compare the levels of bile acids fractions in bile in children with with overweight and obesity according to gallbladder contractile function.

A case-control study was conducted on 120 children aged 6-17 years. All children were divided into 3 groups according to the presence of overweight/obesity and gallbladder function: 1 group - 53 children with overweight/obesity and gallbladder hypokinesia; 2 group - 52 children with overweight/obesity and gallbladder normokinesia; 3 group (control) - 15 children with normal weight and gallbladder normokinesia. Bile acids in bile were evaluated by thin layer chromatography. The presence of liver fibrosis and steatosis was carried out with transient elastometry (FibroScan®502Touch, Echosens, France) and controlled attenuation parameter (CAP) measurement.

Results: The significant increase in the concentration of cholic acid was observed in children with overweight/obesity and gallbladder hypokinesia - in 1,3 times ($p > 0,05$) in comparison to the group 2. There was also a tendency to change the ratio and number of bile acids fractions: the content of taurocholic acid increased almost in 2,5 times ($p > 0,05$), compared with group 2, whereas the glycocholic acid content decreased in 1,3-times ($p > 0,05$), compared with group 2. Changes in bile acid composition of gallbladder's bile in children of the group 1 occurred due to a 1,4-times increase in the production of taurine derivatives relative to glycans. Thus, in group 2, the ratio of taurine derivatives to glycans was 1:2, and in group 1 - 3:2, while increasing the total amount of bile acids in bile. There was an increase in the concentration of all fractions of bile acids in the group 2: taurocholic, taurodeoxycholic and glycocholic - in 1,3 times ($p > 0,05$), glycodeoxycholic by 11% ($p > 0,05$) in comparison to control group. Significantly higher values of liver stiffness and fat content were observed in 1 group patients compared to 2 group (4.6 ± 1.2 kPa and 4.0 ± 0.7 kPa; 250.6 ± 57.4 dB / m and 219.5 ± 33.5 dB / m, respectively ($p < 0.02$)).

Conclusion: Changes in bile acid composition in overweight and obese children according to gallbladder dysfunction indicates the predisposition for the progression of structural changes in the liver and the formation of liver steatosis in children.

Disclosure: Nothing to disclose

P0302

MATERNAL OBESITY INDUCED BY DIFFERENT DIET PROGRAM ALTERS COGNITIVE FUNCTIONS, THE PLASMA LEVELS OF APPETITE HORMONES AND INTESTINAL EXPRESSION OF ADIPOKINES AND ADIPO RECEPTORS 1 AND 2 IN MALE AND FEMALE RAT OFFSPRING

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Introduction: Previous studies have established that maternal health and nutrition have a long-lasting impact on offspring health. Obesity and excessive weight gain during pregnancy are associated with poor pregnancy outcomes such as macrosomia, preterm delivery and greater obesity risk later in life. **Maternal obesity and consumption of a high-fat diet (HFD) in the offspring can exerts the detrimental consequences in offspring cognitive functions.** Recently, maternal consumption of high fat/sucrose diet haD impacted metabolic outcomes and the mesolimbic reward system in dams and offspring.

Aims & Methods: There is no information available whether different diets in maternal obesity including HFD and carbohydrates can influence the appetite hormones and intestinal expression of peptides involved in development of obesity in offspring.

We evaluated the influence of maternal HFD during pregnancy and lactation on the rat offspring plasma concentration of appetite hormones leptin and ghrelin. We also determined the mucosal expression of adiponectin, adiponectin receptors AdipoR1 and AdipoR2. The expression of resistin, the adipokine secreted by immune, epithelial cells, and adipose tissue has been determined. The individually housed pregnant females received standard diet (SD, 64% carbohydrate, 13% fat, 23% protein, 3.4 kcal/g; VRF, UK), HFD (25% carbohydrate, 60% fat, 15% protein, 5.31 kcal/g; C1057), carbohydrate diet (HCD, 70% carbohydrate, 12% fat, 18% protein, 3.77 kcal/g; C1010) or mixed diet (MD, 56% carbohydrate, 28% fat, 16% protein, 3.90 kcal/g; C1011) (Altromin, Germany). Dams were maintained on these diets *ad libitum* during the gestation and lactation periods (21 days). After weaning, offspring was separated according to sex, housed 6 per cage and fed SD. The behavioral tests including the locomotor activity and forced swimming test were performed to determine the immobility time in male and female offspring. At 28 day, offspring was sacrificed and the blood and intestinal biopsies were collected.

Results: The exposure to maternal HFD increased the body weight of males but not females, significantly increased the immobility time in both sexes but had no effect on locomotor activity. In male but not female fed HFD or MD, the expression and plasma leptin levels was significantly elevated ($p < 0.05$), while no difference was recorded in HCD vs. SD. In contrast, plasma concentration of leptin was significantly increased in MD females ($p < 0.05$). The plasma ghrelin was significantly increased in males and females fed MD, but remained unchanged in those fed HFD and HCD. The mucosal mRNA expression for adiponectin and resistin was significantly inhibited in both males and females fed HFD ($p < 0.05$) but not significantly altered by HCD and MD. Exposure of male or female offspring to maternal HFD and MD raised the mRNA expression of AdipoR1 but not AdipoR2 receptors. The maternal HFD decreased serum and hippocampal irisin levels in females on postnatal day 28 and decreased interleukin-1 α content in the hippocampus. However, despite the observed changes in the levels of irisin and IL-1 α in females, further investigations are required to identify the underlying molecular mechanism associated with depressive-like behavior in the offspring of HFD-fed dams.

Conclusion: 1) maternal obesity provokes a long-term depressive-like behavior in male and female offspring and impairment of the offspring central regulation of food intake, and 2) the decreased ratio of adiponectin vs. leptin at maternal HFD during lactation may predispose adult offspring adiposity and metabolic dysfunction in later age.

Disclosure: Nothing to disclose

P0303 WITHDRAWN

P0304 WITHDRAWN

P0305

NOVEL GRAPE-DERIVED PREBIOTIC SELECTIVELY ENHANCES ABUNDANCE AND METABOLIC ACTIVITY OF IBD AND IBS FAECAL BUTYRATE PRODUCING BACTERIA IN AN *IN VITRO* MODEL OF INTESTINAL FERMENTATION

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Introduction: Inflammatory Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS) are two intestinal disorders with unknown aetiology. IBD presents two main forms which are Crohn's disease (CD) and Ulcerative Colitis (UC), whereas IBS is a disorder thought to be of psychosomatic origin. It has been reported recently that bacterial communities present in the colon of patients with either IBD or IBS are structurally different compared to those found in healthy individuals. This dysbiosis mainly consists of a decrease of butyrate producing bacteria and, therefore, recovering of this metabolic group should be at the baseline of any successful treatment
Aims & Methods: The main goal of this work was to test, in a proof of concept, the capacity of a new prebiotic of selected dietary fibre made from grape to balance the dysbiosis found in patients with different intestinal disorders. A preliminary research was conducted using stool samples from patients diagnosed of CD, UC, IBS and healthy subjects, samples were incubated together with this prebiotic and results compared with those obtained by several *in vitro*-digested commercial prebiotics as inulin, grape pectin and grape seed extract (GSPE).

In this proof of concept, 6 faecal samples from healthy subjects, 3 CD, 3 UC and 3 IBS samples were collected by the Hospital Universitari Dr. Josep Trueta. Fresh samples were diluted 1:5 with fermentation buffer and incubated with 200 mg of prebiotic at 37 °C under agitation for 72 h. A blank sample without any fibre addition was used as a procedure control. Total DNA was extracted and the abundance of butyrate-producing bacterial markers: *F. prausnitzii* (Fpra), its two phylogroups (PHGI and PHGII), *Roseburia* spp. (Ros) and *S. variable* (Sva) was analysed by qPCR. Bacterial activity was determined by measuring short chain fatty acids (SCFA) as butyrate, acetate and propionate production by gas chromatography.

Results: All butyrate-producing bacteria analysed increased when fed with the tested new prebiotic. In particular, Ros grew to significantly higher values with respect to the negative control in all tested subjects, except for CD samples, where no improvement was observed. Furthermore, in samples from healthy subjects, the new prebiotic boosted significantly the abundance of Fpra and PHGI (p= 0.001 and 0.019, respectively). The

new fibre showed significantly more efficiency than inulin, grape pectin and GSPE in both stimulating the growth of Ros in all healthy individuals and CD, UC and IBS patients. No significant differences were observed regarding Fpra, PHGI, PHGII, and Sva when comparing the novel prebiotic and the commercial ones.

Fermentation of the tested new prebiotic, produced significantly higher concentrations of SCFA (p < 0.001) when compared to negative control and all other commercial fibres. Acetate was a 241% higher than negative control, followed by butyrate (187%) and propionate (169%).

Conclusion: The studied prebiotic produces an *in vitro* increase of the abundance and enhancement of the metabolism of butyrate-producing bacteria, when compared to commercial prebiotics. These results suggest that this new fibre is a promising prebiotic to be used in promotion of intestinal microbiota restoration at mucosa as a therapeutic strategy towards microbial healing of UC and IBS and as a preventive supplement for healthy individuals.

Disclosure: Nothing to disclose

P0306 WITHDRAWN

P0307 WITHDRAWN

P0308

THE IMPACT OF NUTRITIONAL AND LIFESTYLE FACTORS ON THE INCIDENCE OF COLON DIVERTICULOSIS IN DIFFERENT AGE GROUPS

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Introduction: Diverticular disease (DD) is one of the most common conditions affecting people in developed countries, is often called a "disease of Western Civilization". It gave rise to led to the hypothesis that the increasing incidence of DD may be attributed to modifiable diet and lifestyle factors.

Aims & Methods: The aim of our study was to assess the influence of various lifestyle and nutritional factors on the incidence of colon diverticulosis in different age groups and different locations.

Methods.

The study group involved 58 subjects (33 women and 25 men) with colon diverticulosis (at various stages of the disease - from asymptomatic to acute diverticulitis), aged 33-85 years, hospitalized at the Department of Gastroenterology. Patients were asked to complete a detailed nutritional questionnaire, consisting of over 100 questions, regarding lifestyle and eating habits. In each subject also body mass index (BMI) and waist-hip ratio (WHR) were calculated, as well as anthropometric measurements, body composition tested with Bodystat QuadScan 4000 analyzer.

Results: The incidence of colon diverticulosis increases with age in both sexes. Is also higher in patients with obesity, especially in men.

In the group of younger patients - under 50 years of age, BMI in the group of women bmi was lower - on average - 22.8 kg / m²; in the group of men - 26.7 kg / m². The waist-hip ratio was high - the average 0,98. This relationship is not so visible in the group of younger women. In each group of patients higher body fat amount (MBF) was observed. Interestingly, the hydration rate was worse in both sexes (avg. 55.2%).

A smaller amount of dietary fiber - especially the soluble fraction - was observed in all groups of patients. Analyzing the results of the nutritional

questionnaire, a reduced frequency of consumption: dark bread, pasta, dark rice, cereal, green vegetables, carotene-rich vegetables, fruit, fish, dairy, legumes, nuts, and vegetable oils was found in all groups. The increased frequency of potato and egg consumption in men under 50 years of age was observed and increased consumption of cured meat and red meat in older patients of both sexes.

The amount of fluid consumed was also smaller. Patients consumed processed food much more often, with a lot of salt. In the group of younger people, fast food and energy drinks were more often consumed.

In the group of people over 50 years of age, no differences in the level of education or residence were observed, in the younger group people with higher education, from a large city, dominated. The large number of hours spent by the computer and TV, notably physical activity regardless of body weight was noteworthy. The number of hours of sleep was also very small.

Conclusion:

1. The combine effect of multiple lifestyle and nutritional factors on incidence of diverticulitis incidence is still unclear.
2. Red meat, a small amount of dietary fiber (especially soluble fraction), low physical activity, high body mass index could influence the incidence of diverticulitis but only in the elderly group
3. The obtained results encourage us to further research

Disclosure: Nothing to disclose

P0309

PROTEIN MALNUTRITION CAUSES LONG-LASTING ALTERATIONS IN EPITHELIA-MICROBIOME INTERACTIONS WITH CONSEQUENCES FOR INTESTINAL INFLAMMATION

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Introduction: Protein energy malnutrition (PEM) causes wasting, stunting, neurological defects and an increased susceptibility for pathogenic infections making it one of the leading causes of child mortality worldwide. Supplementation with therapeutic food ameliorates PEM symptoms, yet 10-15% of recipients do not respond to the treatment. Nutritional perturbations such as PEM disturb the homeostatic equilibrium between the intestinal epithelium and its associated microbiota and whether a healthy ecosystem can then be restored is unknown.

Aims & Methods: We aimed to understand on a molecular level how PEM disturbs physiological responses of the intestinal epithelium and the microbiota and to elucidate how this ecological system recovers from PEM with the goal to develop more effective therapeutic interventions. We therefore subjected mice to an acute PEM followed by a recovery period and analysed the temporal effects on the microbiota and host physiology, in particular regarding inflammatory susceptibility.

Results: We found that PEM induced drastic modifications of the gastrointestinal tract but also systemic immunity and metabolism. A single episode of PEM extensively changed the intestinal epithelial transcriptome in response to PEM, in particular Paneth cell-derived antimicrobial functions were depleted. PEM also altered the microbiota composition by enriching for Gammaproteobacteria and Bacteroidaceae while depleting for Actinobacteria and Verrucomicrobia. The functional metagenomic repertoire was characterized by dysregulation of tryptophan metabolism. Importantly, PEM-induced changes in the microbiota and epithelial tran-

scriptome partially remained upon switching to control diet, indicating a molecular “memory effect”. These long-lasting PEM-induced microbiome and transcriptome changes also altered the inflammatory susceptibility in an experimental colitis model *in vivo*. Reduced representation bisulfite sequencing revealed that the PEM transcriptome memory signatures are not caused by changes in DNA-methylation. However, in the absence of a microbiota, germ-free mice showed drastically reduced PEM symptoms and an altered recovery. On-going experiments aim at determining the role of individual host “memory” genes and their epigenetic regulation.

Conclusion: Our data identified alterations in the microbiome and epithelial transcriptome as potential molecular mechanisms underlying the long-lasting physiologic consequences of PEM, thus paving the way to develop novel microbiome-targeted therapeutic interventions for malnutrition.

Disclosure: Nothing to disclose

P0310

ETIOLOGY AND CURRENT MANAGEMENT OF SHORT BOWEL SYNDROME IN ITALY: A PRELIMINARY REPORT FROM AN AIGO SURVEY

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Introduction: Short bowel syndrome (SBS), defined as a small bowel length less than 200 cm due to multiple surgical resections, is the most frequent cause of intestinal failure. Prevalence in adults of this rare condition in Europe is 5-6 per million, data being estimated on reports on home parenteral nutrition, which has been the mainstay of treatment. Italian data are scanty and only few referral centres have a structured approach to SBS.

Aims & Methods: We have conducted a survey among Italian gastroenterologists to assess etiology and management strategies of SBS. All gastroenterologists registered to AIGO (Italian Association of Hospital Gastroenterologists) were invited to fill up a questionnaire reporting data on number of pts with SBS in follow-up, etiology and type of SBS according to ESPEN classification, cases of intestinal failure due to other causes, parenteral/enteral nutrition, venous access and homecare strategies (provided by national service or drug companies). Data on characteristic of the centre (academic or hospital or district clinic) and on the specialty of the treating physician were also recorded. Questionnaires were diffused during national meetings and through the AIGO website.

Results: From October 2018 to October 2019 36/106 centres reported 138 patients with SBS: 64 (46%) Crohn's disease, 34 (25%) surgical complications, 19 (14%) mesenteric ischemia, 7 (5%) familial polyposis, 4 (3%) radiation enteritis and 10 (5%) other etiologies. Of these 65 (47%) receive enteral tube feeding, 44 (32%) parenteral nutrition by PICC / Port-a-Cath, 29 (21%) are on normal diet, without iv supplementation. Most cases, 113 (82%), are followed-up in a general (non academic) hospital, 25 (18%) in a university hospital. Treating physicians are all gastroenterologists, 10 (7%) of whom work in an internal medicine unit.

Conclusion: Participation to the survey was not satisfying, suggesting that the awareness of SBS among gastroenterologists is low and prevalence thus underestimated. Crohn's disease, surgical complications and mesenteric ischemia are the most frequent causes. The knowledge of this condition should increase in view also of the novel therapeutic options with the GLP-2 analogue teduglutide and of the improved life expectancy due to optimization of home parenteral nutrition facilities.

Disclosure: Nothing to disclose

P0311

VITAMIN D SUPPLEMENTATION IN PATIENTS WITH CYSTIC FIBROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Pancreas exocrine insufficiency (PEI) occurs in 85-90% of patients with cystic fibrosis (CF). Lack of pancreas enzyme results in protein and fat malabsorption, failure to thrive, poor weight gain and deficiency in macro- and micronutrients. Despite the routine supplementation, vitamin D deficiency is often seen in CF. D hypovitaminosis can lead to skeletal complications and increases the frequency of pulmonary exacerbations.

Aims & Methods: We aimed to assess the effects of vitamin D supplementation on vitamin D levels, respiratory outcomes and the safety of vitamin D administration in CF.

In this meta-analysis, we included RCTs that compared vitamin D supplementation (any dose, form and duration) with placebo (i.e. 'non-increased dose') in CF patients (regardless of age and comorbidities). We conducted a systematic search in 4 databases: Embase, MEDLINE, CENTRAL and Web of Science. No filters were applied and there were no restrictions based on language, country of origin, and date. In meta-analysis, weighted mean difference (WMD) with 95% confidence interval (CI) were calculated.

Results: Eight RCTs were eligible for inclusion. The intervention group had significantly higher se25OHD levels (WMD 10.48 ng/ml, CI 0.72-20.24 ng/ml). There were no significant differences found in the quantitative synthesis of clinical outcomes, including bone disease-related outcomes, mortality, respiratory and immunological status-related outcomes. All of the included studies had a mean se25OHD below the recommended 30 ng/ml at baseline, while all intervention groups reached this value by the end of the study.

Conclusion: Vitamin D deficiency often results from fat malabsorption caused by PEI, high latitude, poor nutritional intake, reduced exposure to sunlight, impaired activation, and non-adherence to the prescribed vitamin D treatment. In the present meta-analysis, a higher vitamin D dose resulting in significantly greater se25OHD levels did not seem to improve clinical outcomes significantly, this can be due to the heterogeneous outcome choices across the studies, the low sample size and differences in populations.

Disclosure: Nothing to disclose

P0312

RATE AND SEVERITY OF 30-DAY AND 1-YEAR COMPLICATIONS ARISING FROM PERCUTANEOUS ENDOSCOPIC GASTROSTOMY USE

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Introduction: Percutaneous Endoscopic Gastrostomy (PEG) feeding is utilised in patients with exceptionally poor oral intake, such as those undergoing treatment for head and neck cancer or dysphagia. PEG feeding

increases the risk of many complications which are important in pre-insertion counselling and post-insertion management. While some papers have been published on this topic, this is the first UK study to review longitudinal gastrostomy complications since the 2004 NCEPOD audit of PEG deaths and the subsequent changes in practice.

Aims & Methods: Single-centre retrospective chart review of all patients receiving PEG insertion between January 2016 and December 2018. Subgroup analysis compared those who were cared for with professional help vs those who relied on self/family support using chi-squared and Fisher exact analysis.

Results: 306 patients met the inclusion criteria. The mean age at insertion was 67 years. The majority were cared for in their own home (80.4%) by themselves or family (74.8%). 127 were inserted for dysphagia and 165 prophylactically prior to treatment for head and neck cancer.

16.7% had a complication in the first 30 days. The most common complication was pain (45.3%), followed by a weeping/irritated site (17.2%), leaking tube (6.3%) and site infection (6.3%). 50.0% of 30-day complications were "mild" (treated in the community), 48.4% were "moderate" (reviewed in secondary care) and 1.6% were "severe" (required an invasive procedure to rectify).

35.6% experienced at least one complication in the first year. The most common was pain (27.6%), followed by a weeping/irritated site (17.8%), external overgranulation (11.4%) and site infection (11.4%). 53.0% were "mild", 40.5% "moderate" and 6.5% "severe".

The incidence of serious gastric bleeds over the 1-year period was 2.2%, aspiration pneumonia occurred in 3 patients (1.6%) and buried bumper syndrome (BBS) occurred in 1 (0.6%). 30-day mortality for patients post-insertion was 4.2%, with the 10/13 of these falling into the dysphagia group.

Subgroup analysis showed those who relied on self- or family-care had a 63% higher chance of developing at least one complication over a 1-year period compared to those with professional support. This was statistically significant at $p = 0.0177$.

Conclusion: This study represents one of the largest of its kind evaluating the complications arising from PEG insertion. The findings correlate reasonably well with published data.

This study provides valuable data on the rate and severity of complications arising from PEG use and has implications for consenting and counselling patients pre-insertion as well as planning support services and post-insertion management.

References: N/A

Disclosure: Nothing to disclose

P0313

NUTRITIONAL EVALUATION AND MANAGEMENT IN PATIENTS WITH COVID-19 FOLLOWING HOSPITALIZATION IN INTENSIVE CARE UNITS

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Introduction: Among hospitalized patients with COVID 19 pneumonia, up to 32% may require admission in intensive care units (ICU). The aim of this prospective cohort study is to assess nutritional parameters in patients with COVID 19 following ICU.

Aims & Methods: All patients with COVID 19 requiring ICU stay (minimum 14 days) with mechanical ventilation were included after ICU discharge. Recorded parameters at the time of post-ICU rehabilitation unit (PIRU) admission included demographics, body mass index (BMI), weight loss (%), Hand Grip Test (kg), nutrition therapy modalities, and albumin dosage (gr/l). Quantitative parameters were expressed in median and range.

Results: Until May 5th 2020, 11 patients were included (age 58(33-75) years old, and 5 men (45%)). BMI at ICU admission was 25.7 (22.2-33.3) kg/m². Duration regarding ICU stay and ventilation were respectively 29 (25-39) and 22 (13-28) days.

Three patients (27%) required extracorporeal membrane oxygenation and tracheostomy was performed in 5 (45%). During ICU stay, enteral nutrition was administered to all patients through a naso-gastric tube; a percutaneous endoscopic gastrostomy was placed in the ICU in two patients. One patient required complementary parenteral nutrition.

At the time of admission in the PIRU, BMI was 22.9 (19.1-32.9) kg/m² and nutrition dosage was calculated at a median of 2553kcal/day (≥ 28 kcal/kg/day) and 128 gr protein/day (≥ 1.3 gr/kg/day). Weight loss since ICU admission was estimated at 8.3% (4.3%-14%). Post-extubation dysphagia requiring texture adaptation was present in 5 patients (45%). Albumin levels were 30 (26-36) gr/L. Hand-grip was 12 (8-26) kg and 0 (0-20) kg for respectively men and women, reflecting significant sarcopenia.

Conclusion: Critical illpatients with COVID 19 pneumonia are malnourished and have severe sarcopenia following ICU stay despite adequate nutrition management. Optimal nutrition therapy remains crucial during the rehabilitation period.

Disclosure: Nothing to disclose

P0314

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN PEDIATRIC PATIENTS WITH RARE DISEASES IMPROVE NUTRITIONAL STATUS

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Introduction: Enteral nutrition (EN) becomes fundamental in the management of neuromuscular and neurological diseases in children, current guidelines suggest to use a gastrostomy tube or enterostomy tube when the enteral nutrition support exceed 4 weeks.

Aims & Methods: The aim of our study was to evaluate the effect of Percutaneous Endoscopic Gastrostomy (PEG) on nutritional status of paediatric patients affected by rare neuromuscular and neurological diseases, we also considered the complication rate. Data were collected from a retrospective structured database. Eligible patients were less than 18 years old, carrying neurologic diseases that required apposition of PEG for enteral nutrition and medical therapy. In patients aged < 2 years we inserted a 14 Fr or 16 Fr tube while in older patients we inserted a 20 Fr using pull method. The endoscopic technique was performed with anaesthesiologic support in deep sedation and the general anaesthesia was used when needed.

Results: There were 14 males (58.3%) and 10 females (41.7%), average age 56.2 months (CI 95%: 27 - 85.4 months). The diagnosis was Spinal Muscular Atrophy (SMA)1 in 14 patients (58.3%), SMA2 in 1 patient (4.2%), 2 Duchenne's syndrome(8.3%), 1 Ullrich syndrome(4.2%), 2 Steinert syndrome (8.3%), 1 muscular dystrophy(4.2%), 3 undefined diagnosis(12.5%). In 15 patients after 6 months the gastrostomy tube was replaced with a button and for 2 patients the gastrostomy was replaced with a Gastro-jejunal tube after onset of gastro-oesophageal reflux. The time trend of the growth is reported in the following table. The growth achieved statistical significance in patients aged < 2 years. For the children aged >2 years the difference was not statistically significant, probably due to the inadequate sample size. Two patients died during follow up following respiratory complications related to the neurological disease. Major adverse events related to the endoscopic procedure were 2: a buried bumper syndrome and a translocation of internal bumper in the trasversum colon.

	Patients ≤ 2 years old	Patients ≤ 2 years old	Patients >2 years old	Patients >2 years old
Time	Mean Weight kg $\pm$ SD (n. patients)	Mean Height cm $\pm$ SD (n. patients)	Mean Weight kg $\pm$ SD (n. patients)	Mean Height cm $\pm$ SD (n. patients)
0	6.9 $\pm$ 6.3 (13)	68 $\pm$ 8 (10)	16.4 $\pm$ 6.3 (8)	124 $\pm$ 25 (7)
After 3 months	7.8 $\pm$ 2.6 (7)	73 $\pm$ 10 (6)	18.8 $\pm$ 7.9 (6)	131 $\pm$ 27 (5)
After 6 months	9.9 $\pm$ 2.9 (8)	80 $\pm$ 10 (5)	19.2 $\pm$ 6.7 (5)	129 $\pm$ 29 (4)
After 12 months	10.5 $\pm$ 2.9 * (9)	83 $\pm$ 8 (8)	23.15 $\pm$ 5.7 (6)	135 $\pm$ 23 (5)

p value not significant, except for **p=0.022, *** p=0.008

[The time trend of growth after PEG placement]

Conclusion: The endoscopic gastrostomy in children affected by rare neurological and neuromuscular diseases allowed a statistically significant growth, especially for patients aged < 2 years. In our experience the major adverse events were infrequent, in only one case the patient needed surgical treatment.

Disclosure: Nothing to disclose

P0315

NUTRITIONAL STATUS ASSESSMENT AND ASSOCIATED FACTORS FOR UNDERNUTRITION IN PATIENTS WITH DIGESTIVE NEOPLASIA

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Introduction: Digestive cancers remain a serious pathology despite diagnostic and therapeutic progress, requiring a global management that takes into consideration the tumor itself and the impact of the disease on the different aspects of the patient's daily life in order to guarantee a better quality of life. Undernutrition is one of the most dreaded complications of digestive cancers due to its organic and psychological repercussions. The aim of this study was to assess the nutritional status of patients with digestive tumors and to determine associated factors for undernutrition in this population.

Aims & Methods: A prospective study (November 2019-January 2020) including all patients presenting for the management of digestive tumors was performed. A nutritional survey based on the "Mini Nutritional Assessment (MNA)" screening test and anthropometric measurements was carried out. Epidemiological, clinical, biological and histological data were collected and analyzed to research associated factors for undernutrition (SPSS 22.0, p value significant if lower than 0.05).

Results: 49 patients with a mean age of 58 years [18-89] and a sex ratio of 1.1 (53% male, 47% female) were enrolled. Colonic tumors accounted for 43% of all tumors, pancreatic tumors 25%, small bowel neoplasia 12%, liver tumors 8%, rectal tumors 6% and gastric tumors 6%. The histological study concluded in 65.3% of cases to adenocarcinoma, 22.4% carcinoid tumors and 12.2% carcinoma. The extension assessment had shown distant metastases in 32% of cases. 77% of patients had undergone surgery, 10% received chemotherapy and 13% were treated symptomatically.

The WHO Performance Status (PS) assessment showed that 2.2% had a PS=0, 48.9% had a PS=1, 37.8% had a PS=2 and 11.1% had a PS=3. Anorexia was present in 92% of cases while 69% of the patients had a weight loss with an average of 7 kg in 3 months. According to the WHO body mass index (BMI) classification, 12.24% of patients were underweight, 65.30% were normal weight. Brachial circumference (BC) measurement showed that 6.1% of patients were confirmed undernourished (BC< 21 cm), 20.4% were at risk of undernutrition (BC between 21 and 22 cm) and 73.5% had a normal BC (BC>22cm). The measurement of calf circumference (CC) concluded that 24.5% of patients had a poor nutritional status (CC< 31cm). Mini Nutritional Assessment scores showed that 20% of patients had a normal nutritional status, 15% had proven malnutrition and 65% were at risk of malnutrition. The mean calories intake was 816.04 Cal/day with a maximum of 1949.4 Cal/day and a minimum of 119.2 Cal/day. 2% of the patients consumed one meal/day, 22.5% consumed 2 meals/day and 75.5% consumed 3 meals/day.

The statistical study showed that the factors associated with undernutrition were: alcohol consumption (p=0.04), PS (p=0.007) and decreased number of daily meals (p=0.003).

Conclusion: Patients with digestive cancers are susceptible to malnutrition, and in our study alcohol consumption, Performance status and number of meals per day were risk factors for malnutrition. Cancer-related malnutrition must be actively sought in order to ensure adequate management and improve the quality of life of these patients.

Disclosure: Nothing to disclose

P0316 WITHDRAWN

Poster presentations

IBD

IBD

09:00-19:00 / Poster Exhibition

P0317

THE IMMUNE CELL LANDSCAPE OF POUCHITIS AFTER ILEAL POUCH-ANAL ANASTOMOSES FOR INFLAMMATORY BOWEL DISEASE

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Introduction: Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is a common surgical procedure in patients with inflammatory bowel disease (IBD) refractory to medical therapies. Pouchitis, the most common complication of IPAA, is inflammation of the ileal pouch reservoir of unknown etiology.

Aims & Methods: To define the immune landscape and develop mechanistic hypotheses of pouchitis, we analyzed tissues from patients with and without pouchitis and from patients with UC using single-cell RNA sequencing (scRNA-seq). We prospectively obtained intestinal mucosal pinch biopsies from IBD patients with IPAA and ulcerative colitis (UC) undergoing endoscopy for disease activity assessment between 2018 and 2019. Demographic, clinical, and disease-related data were collected. The endoscopic findings of the pouchitis disease activity index (PDAI) were used to categorize patients into pouchitis cohorts. All UC patients had endoscopic evidence of inflammation. The landscape and gene expression of pouch lamina propria cells using scRNA-seq was performed and compared between patients with and without pouchitis, and with actively inflamed UC.

Results: We obtained biopsies from 15 patients with a pouch and 13 patients with active UC. Of patients with a pouch, 14 (93%) underwent an IPAA for medically refractory disease and, based on the endoscopic PDAI, 10 (67%) had pouchitis. Of patients with UC, the majority had left-sided or extensive colitis (n= 11, 85%) and a Mayo 3 endoscopic subscore (n= 11, 85%). In total, we identified 18,375 cells from UC, 16,878 cells from normal pouches, and 20,678 cells from pouchitis. Major immune subsets were identified including five myeloid clusters, 5 B cell clusters, and 12 T cell clusters. Generally, myeloid populations were higher in active UC (2.0%) and pouchitis (1.4%). In particular, the percentage of SOX4+ and MAFA+ myeloid cells was significantly higher (p<0.001) in both inflamed UC (1.8%) and pouchitis (1.3%) compared to uninflamed pouches (0.2%). Clustering of T cell subsets revealed a predominance of FOXP3+ T cells in active UC (8.0%) and pouchitis (7.2%) compared to normal pouches (3.9%, p<0.01). The percentage of SOX4+/MAFA+ myeloid cells and FOXP3+/BATF+ T cells were linearly related with the presence of inflammation in active UC and pouchitis (p= 0.006).

Conclusion: In this study of the cellular landscape of pouch and UC lamina propria cells using scRNA-seq, there were major differences in immune subsets. Myeloid populations and FOXP3+ T cells were enriched in active UC and pouchitis compared to normal pouches, suggesting that mechanisms of mucosal inflammation in pouchitis may mimic that of UC.

Disclosure: Nothing to disclose

P0318

INFLIXIMAB RESPONSE IN INFLAMMATORY BOWEL DISEASES IS LINKED TO INTERACTION BETWEEN MUCOSAL MICROBIOTA COMPOSITION AND HOST GENE-EXPRESSION

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Introduction: Even though anti-TNF therapy significantly improves the rates of remission in inflammatory bowel disease (IBD) patients, there is a noticeable subgroup of patients who do not respond to treatment. Dysbiosis emerges as a key factor in IBD pathogenesis.

Aims & Methods: The aim of the present study is to profile changes in the gut microbiome and transcriptome before and after administration of the anti-TNF agent Infliximab (IFX) and investigate their potential to predict patient response to IFX at baseline.

Mucosal biopsy samples from 20 IBD patients and 9 healthy controls (HC) were examined for differences in microbiota composition (16S rRNA gene sequencing) and mucosal gene expression (RT-qPCR) at baseline and upon completion of IFX treatment, accordingly, via an in silico pipeline.

Results: Significant differences in microbiota composition were found between IBD and HC groups. Several bacterial genera, which were found only in IBD patients and not HC, had their populations dramatically reduced after anti-TNF treatment regardless of response. Alpha and beta diversity metrics showed significant differences between our study groups. Correlation analysis revealed 6 microbial genera associated with differential expression of inflammation-associated genes in IFX treatment responders at baseline.

Conclusion: This study shows that IFX treatment has a notable impact on both the gut microbial composition and the inflamed tissue transcriptome in IBD patients. Importantly, our results identify enterotypes that correlate with transcriptome changes and help differentiate IFX responders versus non-responders at baseline, suggesting that, in combination, these signatures can be an effective tool to predict anti-TNF response.

Disclosure: Nothing to disclose

P0319

EXPOSURE TO AN INFLAMMATORY MIX RE-INDUCES INFLAMMATION IN ORGANOID OF ULCERATIVE COLITIS PATIENTS, INDEPENDENT OF THE INFLAMMATORY STATE OF THE TISSUE OF ORIGIN

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Introduction: Patient-derived intestinal organoids provide a powerful tool to unravel mechanisms underlying inflammatory bowel disease (IBD). Recently, we showed that organoids derived from inflamed regions in ulcerative colitis (UC) patients lose their inflammatory phenotype during *ex vivo* culture and were indistinguishable from organoids of non-inflamed regions in these patients [1].

Aims & Methods: To study UC in an *ex vivo* model, we hypothesized that inflammation should be re-induced towards levels corresponding to the *in vivo* situation. In addition, we aimed to elucidate if organoids derived from inflamed regions are more sensitive towards inflammatory stimulation, compared to organoids from non-inflamed regions of UC patients and non-IBD controls. Biopsies were obtained from 8 patients with active UC (endoscopic Mayo score of ≥ 2), both in inflamed and non-inflamed regions, and in 8 non-IBD controls. Crypts were isolated and cultured as organoids for at least four weeks. Organoids were subjected to a predefined inflammatory mix (MIX: 100 ng/ml TNF- α , 20 ng/ml IL-1 β , 1 μ g/ml Flagellin) or medium only (CTRL) for 24 hours. RNA was extracted from organoids for RNA sequencing by Lexogen QuantSeq for Illumina. Differential gene expression and pathways were studied through DESeq2 and Ingenuity Pathway Analysis (False discovery rate < 0.05).

Results: Prior to inflammatory stimulation, principal component analysis (PCA) demonstrated separate clustering between organoids derived from non-IBD controls and UC patients. Exposure to the inflammatory mix induced transcriptional activation of inflammatory genes (*CXCL1*, *DUOX2*, *IL1 β* , *IL8*, *IL23 α* ,... all $p < 0.001$) and pathways in all conditions. However, organoids of non-IBD controls clustered separate from organoids of UC patients. Within organoids of UC patients (inflamed vs non-inflamed origin), we observed no differentially expressed genes after inflammatory stimulation but organoids clustered per patient instead. Inflammatory markers in UC organoids reached transcriptional expression levels (*CXCL1*, *CXCL2*, *IFNGR1*, *IL1 β* , *DUOX2*,...) and activated pathways (antigen presentation, interferon signaling, granulocyte adhesion and diapedesis) similar to those observed in crypts derived from inflamed biopsies.

Conclusion: Inflammation can efficiently be (re-)induced in organoids from both UC and non-IBD origin. However, a different response was observed between organoids of non-IBD and UC origin. Of note, in UC organoids the state of inflammation in the source tissue was irrelevant. In conclusion, we showed that it is essential to re-induce inflammation in patient specific organoids, but there is no need to obtain biopsies from inflamed regions.

References: [1] <https://doi.org/10.1093/ecco-jcc/ijy222.010>

Disclosure: • Ferrante M. : - Research grant: Amgen, Biogen, Janssen, Pfizer, Takeda - Consultancy: Abbvie, Boehringer-Ingelheim, Janssen, MSD, Pfizer, Sandoz, Takeda - Speakers fee: Abbvie, Amgen, Biogen, Boehringer-Ingelheim, Falk, Ferring, Janssen, Lampro, MSD, Mylan, Pfizer, Takeda • Vermeire S. : - Research grants : MSD, AbbVie, Takeda, Pfizer, Janssen - Consultancy: AbbVie, MSD, Takeda, Ferring, Genentech/Roche, Shire, Pfizer Inc, Galapagos, Mundipharma, Hospira, Celgene, Second Genome, Progenity, Lilly, Arena, GSK, Amgen, Ferring, Gilead and Janssen - Speak-

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P0320

IDENTIFICATION OF CONSTITUTIVE MODIFICATIONS IN PLASMA CELLS AND B LYMPHOCYTES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Plasma cells (PC) and B lymphocytes (BL) are a source of immunoglobulins (Ig), being IgA essential for intestinal homeostasis. An unbalanced intestinal Ig production has been described in inflammatory bowel disease (IBD). Nevertheless little is known about the role of mucosal Ig-producing BL and PC in IBD, reason why we decided to study them.

Aims & Methods: The aim of this study was to identify alterations in the proportions and phenotypes of BL and PC in patients with IBD. We included 12 healthy controls -HC-, 10 patients with ulcerative colitis (3 active -aUC- and 7 quiescent -qUC-) and 10 patients with Crohn's disease (3 active -aCD- and 7 quiescent -qCD-). Disease was located in the distal colon in all patients, although the quiescent ones had no inflammation (Endoscopic Mayo=0; SES-CD=0-1). Distal colon biopsies were collected together with peripheral blood. Mucus layer and epithelial barrier was removed from the biopsies and lamina propria mononuclear cells were harvested using the "walk-out" protocol. Peripheral blood mononuclear cells were obtained after ficoll centrifugation. In both cases, cells were stained with specific antibodies, acquired in a FACSCanto II cytometer, and analysed with FlowJo. Median percentage of PC and BL (and their subsets) relative to each tissue were calculated and compared using non-parametric statistics, considering statistically significant $p < 0.05$.

Results: The proportion of plasmablasts, blood-precursors of PC, was higher in the blood of active IBD patients (HC: 0.8%; aUC: 5.3%; aCD: 3.4%). Even though there were no differences in the colonic proportion of PC between the study groups, there was a constitutive lower proportion of IgA-producing PC in IBD, irrespective of its type (UC or CD) or presence of inflammation (HC: 88%; qUC: 55%; aUC: 38%; qCD: 70%; aCD: 44%). Moreover, aCD patients also showed a significantly higher proportion of IgM-producing PC (HC: 6% vs aCD: 10%), and a higher proportion PC expressing CD19 compared both to HC and qCD (HC: 43%; qCD: 52%; aCD: 74%). The proportion of BL and their subsets did not show differences between the study groups, neither in blood nor in colon. However, in UC patients, some circulating subsets displayed a lower proportion of cells expressing the gut-homing integrin b7: naïve BL (HC: 11.5%; qUC: 2.9%; aUC: 0.6%) and IgM memory BL type CD27+ (HC: 43%; qUC: 30%; aUC: 23%) and also CD27- (HC: 32% vs aUC: 5%).

Conclusion: IBD patients have a diminished percentage of colonic IgA-producing PC, which is irrespective of the type of IBD or the inflammatory status; this reduction could compromise the correct microbiota regulation in IBD. The reduction of the percentage of b7-expressing BL in the blood of UC patients could potentially point to a specific pathogenic mechanism of UC.

Disclosure: Nothing to disclose

P0321

NON-SUPPRESSIVE FOXP3⁺ T HELPER CELLS, BUT NOT REGULATORY T CELLS, ARE INCREASED IN COLLAGENOUS COLITIS MUCOSA

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Introduction: Increased frequencies of T regulatory (Treg) cells, key players in immune regulation, have been reported in inflammatory bowel diseases, including collagenous colitis (CC). However, traditional Treg identification techniques might have misinterpreted the frequencies of Treg cells in CC. Thus, we investigated the presence of genuine Treg cells in CC. **Aims & Methods:** Treg cells were analysed in mucosal and peripheral blood samples of CC patients before and during treatment with the corticosteroid drug budesonide, and in healthy controls. Samples were analysed by flow cytometry by classifying CD3⁺CD4⁺ cells as activated FoxP3^{high}CD45RA⁺ Treg cells, resting FoxP3^{dim}CD45RA⁺ Treg cells, and non-suppressive FoxP3^{dim}CD45RA⁺ T helper cells. Traditional gating strategies that classified Treg cells as CD25^{high}CD127^{low}, FoxP3⁺CD127^{low} and CD4⁺CD25⁺FoxP3⁺ were also used to facilitate comparison with previous studies.

Results: Activated and resting Treg cell numbers did not change in active CC mucosa or peripheral blood and were not affected by budesonide treatment. Instead, non-suppressive FoxP3^{dim}CD45RA⁺ T helper cells were increased in active CC mucosa, and budesonide contributed to restore them to normal levels. In contrast, traditional Treg cell gating strategies resulted in increased Treg cell numbers in active CC mucosa. No alterations were found in peripheral blood samples, independently of patient treatment or gating techniques.

Conclusion: CC fails to trigger a Treg response. Previously reported increase of Treg cells is a result of incomplete Treg phenotyping which included non-suppressive FoxP3^{dim}CD45RA⁺ T helper cells. Since budesonide did not affect Treg numbers, its therapeutic effect in CC might involve alternative mechanisms.

Disclosure: Nothing to disclose

P0322

ULCERATIVE COLITIS: CHARACTERISTICS OF INTESTINAL MICROBIOTA IN RUSSIAN POPULATION

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Introduction: Inflammatory bowel diseases (IBD) are chronic multifactorial diseases characterized by partially unclear pathogenic mechanisms including changes in intestinal microbiota. Can dysbiosis be one of the causes of the disease or is it a consequence of it?

Aims & Methods: This study aimed to evaluate the composition of the gut microbiota in various forms of ulcerative colitis (UC) by real-time polymerase chain reaction (PCR) and to compare it with a control group. 70 cases with UC were selected (43 female - 61.4% and 27 male - 38.6%) with a median age of 40±14.4 years (range 18-69). The duration of the disease was 7.22±6.9 years (range 0.5-38).

Extensive colitis was diagnosed in 78.6% cases (n=55), left-sided colitis - 21.4% (n=15). Acute UC was found in 3 (4.3%) patients, relapsing course of the disease in 29 (41.4%) and remitting course in 38 (54.3%) patients. The activity of UC (Truelove-Witts classification) was variable: mild - 38 (54.3%), moderate - 14 (20%), and clinical remission - 18 (25.7%). 50 non-IBD patients were included in the control group.

Real-time PCR diagnostics of studied samples was carried out using a "DTprime" (Detecting Thermocycler) ("DNA-Technology, Research&Production", LLC, Protvino, Russia). Analysis was completed including the non-parametric Mann-Whitney test, with p < 0.05 deemed to be indicative of statistical significance.

Results: Using real-time PCR, 30 groups of microorganisms from 7 phyla (*Firmicutes*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*, *Fusobacteriaceae*, *Verrucomicrobia*, and *Euryarchaeota*) were identified. According to the results of the total absolute values of bacteria, phyla are distributed in the following order: in the group of UC patients - *Firmicutes* (26.40), *Bacteroidetes* (13.54), *Proteobacteria* (9.76), *Actinobacteria* (5.64), *Fusobacteriaceae* (1.04), *Verrucomicrobia* (0.60), and *Euryarchaeota* (0.00) log(Genome-Equivalent/sample) (GE/sample), in the non-IBD control group - *Firmicutes* (20.13), *Proteobacteria* (13.60), *Bacteroidetes* (10.55), *Actinobacteria* (5.11), *Verrucomicrobia* (2.14), *Fusobacteriaceae* (1.61), and *Euryarchaeota* (0.67) log(GE/sample).

The total bacterial mass (TBM) of biopsies of UC patients (4.470) is less compared to the TBM of the controls (5.010) (p < 0.05) log(GE/sample). *Bacteroides* genus (-0.387) is the main representative of microbiota in the UC group compared with the control group (-0.720) (p < 0.05), where *Clostridium coccoides* (0.024) dominates (p < 0.05). Amount of *Clostridium leptum* gr+ (-0.641), *Streptococcus* spp (-0.944), *Bifidobacterium* spp (-1.401), *Parabacteroides* spp (-1.331), *Lactobacillaceae* (-2.866), *Staphylococcus* spp (-2.424), *Enterococcus* spp (-2.963) log(GE/sample) is higher in UC patients (p < 0.05).

When comparing the representation of *Akkermansia muciniphila*, *Clostridium difficile*, *Coriobacteriia*, *Sutterella wadsworthensis*, *Prevotella* spp, *Erysipelotrichaceae*, and *Escherichia coli*, there was no significant difference between the groups (p > 0.05).

Conclusion: In Russian population of patients with UC three bacterial phyla (*Firmicutes*, *Bacteroidetes*, and *Proteobacteria*) dominate in the intestinal microbiota; low bacterial content (less than 10⁵) of biopsies, probably due to the presence of chronic inflammation; *Bacteroides* genus is

the most prevalent, what is a possible reflection of mucin degradation as a carbon source; no convincing data on the participation of *Akkermansia muciniphila*, *Clostridium difficile*, *Prevotella spp.*, and *Escherichia coli* in the pathological process.

Disclosure: Nothing to disclose

P0323

TRANSCRIPTIONAL CHANGES AFTER BUDESONIDE TREATMENT IN COLLAGENOUS COLITIS PATIENTS

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Introduction: Collagenous colitis (CC) is a common inflammatory bowel disease that mainly manifests through debilitating watery diarrhoea. Treatment with the glucocorticoid budesonide is effective to induce and maintain clinical remission in most cases, however, its specific mechanisms of action in CC are unknown. To understand how budesonide restores homeostasis in the gut, we performed genome-wide RNA sequencing analysis (RNA-seq) of budesonide treated and untreated mucosa from CC patients.

Aims & Methods: We collected colonic biopsy samples from CC patients before and after achievement of clinical remission with budesonide (9 mg/d for 8 weeks, n=9), as well as biopsies from healthy controls (n=13). Laser capture microdissection was used to isolate intestinal epithelial cells (IEC). Total RNA was isolated from bulk biopsies and IEC for library construction and RNA-seq. Whole genome expression data was processed using the R statistical software, and analysed by linear models with least square regression, empirical Bayes moderated t statistics, gene-set enrichment analysis (GSEA) and gene-set variation analysis (GSVA). Results were corrected using the Benjamini-Hochberg FDR method, with an adjusted *p* value < 0.05 considered to be statistically significant. Results were validated in tissue samples from the same patients by immunohistochemistry (IHC).

Results: Active CC displayed an enrichment in gene pathways related to antigen folding and presentation, response to interferon, response to lipopolysaccharide and bacteria, apoptosis and replication mechanisms, and had an imbalanced mitochondrial metabolism compared to healthy controls. Budesonide treatment affected DNA regulation processes as well as gene expression, protein synthesis and trafficking, including genes involved in the immune response. Estimations of infiltrating immune cells performed by GSVA indicated a possible role for professional antigen-presenting cells (i.e. dendritic cells) in CC pathogenesis and budesonide effects.

Even though the CC mucosa is macroscopically intact, microdissected IEC RNA-seq analysis revealed substantial changes in IEC transcriptional programme. GSVA suggested a modified activity in crypt cells that might involve stem and Paneth-like cells. Quantification of Ki67 proliferation marker extension revealed an increased IEC proliferation in active CC that

was partially restored by budesonide. IEC might also play a role in luminal antigen presentation since HLA-C was more expressed in active CC than in budesonide-treated CC and control IEC.

Conclusion: Our analyses confirm that the immune response is increased in collagenous colitis, suggesting a role for dendritic cells and bacterial antigen presentation. We also identified an altered transcriptional programme in intestinal epithelial cells, including a misbalance of cell proliferation. Budesonide decreases the gene expression of these processes in both stromal and epithelial cells. Further study of the transcriptional landscape of CC may reveal additional pathomechanisms and therapeutic vulnerabilities for this common, debilitating inflammatory bowel disease.

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P0324

THE JAK-3 AND TYK-2 / STAT PATHWAYS ARE ACTIVATED IN MODERATE TO SEVERE ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is a chronic, progressive and disabling disease with a complex pathology of unknown aetiology influenced by genetic, environmental and microbiota factors that lead to an immunological and inflammatory response in the colon. Janus Activate Kinase (JAK) family plays a key role in modulating the adaptive and innate inflammatory response. The JAK/STAT pathway involvement in UC has been demonstrated in both animal models and human studies. Thus, overexpressed JAK-3 has been detected in the intestine of patients with UC, suggesting a key role in their pathophysiology and the inhibition of TYK-2 in animal models resulted in an improvement of the disease, which would explain its implication in the inflammatory process. We hypothesize here that there could be an activation of JAK-3 and TYK-2 signalling pathways in UC patients.

Aims & Methods: Thus, we aimed to detect the activation of both signalling pathways by means of western-blot studies in UC patient samples.

A prospective, observational single-center study was designed. Inclusion criteria were adult patients with endoscopic active UC (more than Mayo-0) confirmed in a programmed colonoscopy. All patients signed the informed consent. Samples were obtained from overstock of routine biopsies in the more severe segment affected of the large bowel. Tissues were homogenized and processed in order to obtain cell lysates by employing RIPA buffer and ultrasounds. The degree of activation of the JAK-3 and TYK-2 pathways was measured by detecting the phosphorylation of both targets as well as of STAT1, STAT3, STAT4, STAT5 and STAT6 through Western Blot by employing specific antibodies for total and phosphorylated proteins.

Results: 19 UC patients were consecutively included. Mean age was 46 years old. 53% were female, 47% were extensive colitis (E3) and 53% left-side colitis (E2). Regarding endoscopic activity, 26% had Mayo-1, 53% Mayo-2, and 21% Mayo-3. Immunoreactive bands for both phosphory-

lated JAK-3 and TYK-2 were detected in the biopsies from UC patients, evidencing that colonic inflammation leads to an activation of both targets. The study of STATs phosphorylation showed immunoreactive bands for phosphorylated forms of STAT1, STAT3, STAT4, STAT5 and STAT6 confirming the activation of both signalling-pathways in these patients. The percentage of immunoreactive bands observed in biopsies was higher in patients with a higher Mayo endoscopic score.

Conclusion: The developed translational workflows involving basic/clinical research confirm the activation of both JAK-3 and TYK-2-dependent signalling pathways in UC patients. Both JAK3 and TYK2, as well as their downstream target proteins (STAT1, STAT3, STAT4, STAT5 and STAT6) showed to be activated in UC patient samples. The developed methodology allows studying the target engagement for future JAK-3/ TYK-2 inhibitors employed in clinical trials.

Disclosure: Nothing to disclose

P0325 WITHDRAWN

P0326

NOVEL APPROACH TO BIND AND SPECIFICALLY DETECT FIMH-EXPRESSING *E. COLI* USING HEPTYLMANNOSE-FUNCTIONALIZED CELLULOSE IN THE CONTEXT OF CROHN'S DISEASE

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Introduction: Adherent-Invasive *Escherichia coli* (AIEC) strains isolated from Crohn's disease (CD) patients are able to adhere to and to invade intestinal epithelial cells. FimH adhesin, a mannose binding lectin located at the tip of type 1 pili, is involved in the cell adhesion process. AIEC bacteria share specific allelic variants in *fimH* gene leading to an increased adhesion capacity. This high adhesion phenotype was selected to develop an anti-adhesive treatment against AIEC, as well as a rapid method to detect AIEC.

The potent FimH antagonist heptyl-mannose (HMan) was grafted on cellulose nanofibers (CN) or on cellulose paper (CP) in order to generate therapeutic and diagnostic tools specifically targeting AIEC.

Aims & Methods: HMan was grafted by click chemistry techniques on CN (HMan-CN) or on CP (HMan-CP). Non-grafted or heptyl-glucose-grafted CN or CP were synthesized as controls. HMan-CN was studied for its anti-adhesive effect on intestinal epithelial cells T84 infected with AIEC LF82. *In vivo*, HMan-CN was orally administered (30 mg/kg) to CEABAC10 transgenic mice previously infected with LF82. HMan-CP (27 mm² calibrated papers) was assessed for its ability to bind AIEC LF82, AIEC LF82- Δ *fimH* or *E. coli* K12-C600 in solution. Sensibility and specificity of the detection method were determined in different biological fluids: fecal suspensions and homogenized intestinal biopsies (mouse or human).

Results: Contrary to non-grafted or glucosides-grafted CN, HMan-CN significantly decreased AIEC LF82 adhesion to T84 cells at 10 μ M and nearly abrogated bacterial adhesion at 100 μ M. Anti-adhesive property of HMan was not modified when ligand was grafted on CN. *In vivo*, administration of HMan-CN to CEABAC10 mice favored AIEC elimination from the gut. Concerning the diagnostic strategy, HMan-CP efficiently captured AIEC LF82 bacteria in solution (12.65% of total bacteria bound to paper) contrary to LF82- Δ *fimH* mutant and *E. coli* K12-C600 (1.27% and 1.87% respectively). It demonstrates that bacterial binding to CP is fully promoted by FimH and

that HMan-CP is able to selectively discriminate a *E. coli* strain displaying a high-binding affinity variant of FimH (LF82) from a FimH harboring by a non-pathogenic *E. coli* K12.

Conclusion: Currently, AIEC detection in CD patients is long and fastidious. In this work, we have developed the first paper sensor that selectively and rapidly binds AIEC in solution. This new diagnostic tool could facilitate identification of AIEC-carrying patients to guide them towards personalized therapies targeting AIEC bacteria. Anti-adhesive treatment based on HMan-CN is a promising example of anti-AIEC treatment, specifically targeting one possible trigger of intestinal inflammation.

Disclosure: Nothing to disclose

P0327

COLONIC ORGANIDS FOR THE INVESTIGATION OF CLINICAL RESPONSIVENESS TO ANTI-TUMOR NECROSIS FACTOR AGENTS IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Although anti-tumor necrosis factor alpha (TNF α) agents have markedly improved the treatment of inflammatory bowel diseases (IBD), many patients do not respond to anti-TNF α therapy. Predicting responsiveness to anti-TNF α therapy is critically important to directly improve IBD outcomes. Clinical characteristics and genetic markers of anti-TNF response have had limited predictive capacity. A goal in precision medicine is to use patient-derived specimens to predict disease outcomes.

Aims & Methods: We aimed to use precision medicine to create an ex vivo model of ulcerative colitis (UC) using colonic organoids to investigate responsiveness to anti-TNF α therapies. Clinical data and colonic pinch biopsies were prospectively obtained from patients with UC undergoing colonoscopy for disease activity assessment. Based on clinical data and endoscopic findings, patients were categorized into those naïve, responsive, or refractory to anti-TNF α agents. For organoids, colonic crypts from inflamed or uninfamed segments were isolated and cultured in a standardized fashion. Organoids were embedded in 10 μ l of Matrigel at 4,000-7,000/ml and 40-70 organoids were cultured in 96-well plates in triplicate with or without 10-20ng/ml human(h) interferon gamma (IFN γ) and 20-40ng/ml hTNF α . Susceptibility as a proxy for responsiveness was evaluated by percent of viable organoids determined by daily quantification of the number of intact organoids.

Results: Colonic organoids were created from 18 UC patients (9 naïve, 4 responsive, and 5 refractory to anti-TNF α agents). Compared to naïve and responsive, patients refractory to anti-TNF α agents had a longer median duration of disease (9 years vs. 4 naïve, 3 responsive) and were more likely to have extensive colitis (80% vs 11% naïve, 50% responsive), an elevated median CRP (38mg/dL vs. 2mg/dL naïve, 5mg/dL responsive), and a Mayo 3 endoscopic subscore on endoscopy (40% vs. 22% naïve, 25% responsive). Colonic organoids derived from anti-TNF α responsive patients demonstrated susceptibility to hIFN γ and hTNF α , with a significant decrease in percent of viable organoids at 96 hours (24% hIFN γ , 43% hTNF α vs 78% carrier protein), whereas organoids derived from anti-TNF α refractory patients demonstrated susceptibility to hIFN γ and resistance to hTNF α (46% hIFN γ , 77% hTNF α vs 85% carrier protein; Table). Colonic organoids derived from patients naïve to anti-TNF α agents were distinguished by susceptibility to hTNF α consistent with viability results from either responsive (41% hIFN γ , 54% hTNF α vs 81% carrier protein) or refractory patients (47% hIFN γ , 83% hTNF α vs 94% carrier protein).

Reagent	Anti-TNFα Responsive (n=4)	Anti-TNFα Refractory (n=5)	Anti-TNFα Naïve with hTNFα-resistance (n=3)	Anti-TNFα Naïve with hTNFα-susceptibility (n=6)
Carrier protein	78 ± 14	85 ± 11	94 ± 11	81 ± 6
hTNFα 20ng/ml	54 ± 17	73 ± 15	85 ± 8	57 ± 13
hTNFα 40ng/ml	43 ± 13	77 ± 14	83 ± 9	54 ± 11
hIFNγ 10ng/ml	22 ± 9	41 ± 12	50 ± 9	44 ± 8
hIFNγ 20ng/ml	24 ± 10	46 ± 13	47 ± 9	41 ± 12

[Organoid viability (% ± standard deviation) at 96 hours]

Conclusion: Colonic organoids derived from patients with UC naïve, responsive, or refractory to anti-TNFα agents were differentially susceptible to hTNFα. Clinical responsiveness to anti-TNFα agents reflected organoid viability against hTNFα. These data suggest that organoids from naïve patients with susceptibility to hTNFα may predict clinical efficacy of anti-TNFα therapy or disease severity. Employing precision medicine, intestinal organoids may be a clinically useful ex vivo model of IBD for investigating responsiveness to IBD therapies.

Disclosure: Nothing to disclose

P0328

SHORT DISEASE DURATION AND SUPERFICIAL PENETRATION WITHIN THE ILEAL WALL ARE ASSOCIATED TO M1 MACROPHAGES INFILTRATION AND ACTIVATION IN ILEOCOLONIC CROHN'S DISEASE

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Introduction: Impaired intestinal barrier function and innate immunity are demonstrated to have a role in Crohn's disease (CD). LPS and IFNγ polarize macrophages towards the M1 phenotype, which induces secretion of large amounts of cytokines such as IL-1-β, TNFα, IL-12, IL-18 and IL-23 [1]. Surgical treatment is required in about 70% of CD patients during their life and early surgery seem to lead to a lower recurrence rate [2]. However, the underlying mechanism of early inflammation in Crohn's disease is unknown.

Aims & Methods: The aim of the study is to analyze the immune microenvironment in ileal wall according CD duration and extension within the small bowel wall. Ninety-six consecutive CD patients who underwent ileo-colonic resection were enrolled. Mucosal samples were obtained from both healthy and inflamed ileum. Clinical records with pre- and post-operative details were retrieved. Fibrosis grade was evaluated with an ad hoc pathological score. CD68, CD163 and iNOS were evaluated with immunohistochemistry. Expression of TLR2, TLR4, TLR5, HBD1, HBD2, HBD3, HD5 and HD6 was quantified through Real-Time qPCR. Concentrations of Eotaxin-1, ICAM-1, IL-1α, IL-1β, IL-1ra, IL-12p40, IL-12p70, IL-15, IL-17, IL-23, MMP-3, SCF, VEGF were determined with immunometric assay. Clinical recurrence was defined as Harvey-Bradshaw Index (HBI) ³8 (moderate-to-severe activity). Comparisons and correlations were carried out with non-parametric tests.

Results: CD duration inversely correlated with IFNγ concentration in the ileal mucosa (r=-0.346, p=0.043) with iNOS+ macrophages (M1) in the ileal wall (r=-0.667, p=0.012), and with the depth of neutrophil granulocytes infiltration within the bowel (r=0.314, p=0.026). Similarly, also TNFα con-

centration in healthy ileal wall tended to inversely correlate with disease duration (r=0.29, p=0.09). Moreover, iNOS+ macrophages (M1) infiltration inversely correlated with the depth of neutrophil granulocytes infiltration within the bowel (r=0.347, p=0.046).

Conclusion: In patients with ileocolonic CD, M1 macrophages infiltration, activation and secretion are associated to short duration of disease and superficial inflammation within the ileal wall. These data suggest that the beginning of the inflammation in CD may be M1-macrophages driven.

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P0329

IDENTIFICATION OF RELEVANT PATIENT REPORTED OUTCOMES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE - LISTEN I

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Introduction: Several patient reported outcomes (PRO) have been established and are widely used in the assessment of patients with inflammatory bowel disease (IBD). However, only limited data are available which PRO were experienced by and are most relevant for IBD patients.

Aims & Methods: A review of IBD-related disease scores led to the identification of 16 different PRO categories (9 symptoms and 7 impacts) that characterize the patient's disease burden. In a cross-sectional study in three German practices with a gastroenterological focus, a digital patient survey was carried out to determine the self-experience and the relevance of these PRO categories by pair-wise comparison.

Results: 60 patients with Crohn's disease (56.7% women; mean age 40.6 years; mean disease duration 12.4 years) and 60 patients with ulcerative colitis (51.7% women; mean age 37.3 years; mean disease duration 9, 0 years) participated in the patient survey.

All pre-defined symptoms and impacts with the exception of nausea were experienced by at least 50% of patients (see Table 1). Urgency and pain were the two most important symptoms for Crohn's Disease patients with similar ratings for relevance. Urgency was also the most important symptom for patients with ulcerative colitis, followed by stool frequency. Nausea was the least relevant symptom. Most important impacts in both patient groups were general well-being followed by social activities, while sexual activity was the least relevant symptom.

Conclusion: Self-Experience of symptoms and their impacts was high and largely similar for both disease groups except for rectal bleeding and nausea. The relevance of symptoms was different for patients with Crohn's disease and ulcerative colitis, while relevance of impacts was similar for both patient groups.

Disclosure: Nothing to disclose

	Crohn's disease n (%)	Ulcerative colitis n (%)	Total n (%)
Total	60 (100.0)	60 (100.0)	120 (100.0)
Symptoms			
Rectal bleeding	36 (60.0)	58 (96.7)	94 (78.3)
Urgency	52 (86.7)	55 (91.7)	107 (89.2)
Fatigue	47 (78.3)	51 (85.0)	98 (81.7)
Flatulence	53 (88.3)	45 (75.0)	98 (81.7)
Weight	47 (78.3)	42 (70.0)	89 (74.2)
Night symptoms	36 (60.0)	41 (68.3)	77 (64.2)
Pain	56 (93.3)	44 (73.3)	100 (83.3)
Stool frequency	52 (86.7)	56 (93.3)	108 (90.0)
Nausea	33 (55.0)	19 (31.7)	52 (43.3)
Impact of symptoms			
Daily activities	45 (75.0)	43 (71.7)	88 (73.3)
Depression/anxiety	36 (60.0)	39 (65.0)	75 (62.5)
Work productivity	47 (78.3)	46 (76.7)	93 (77.5)
General wellbeing	53 (88.3)	55 (91.7)	108 (90.0)
Emotional distress	45 (75.0)	44 (73.3)	89 (74.2)
Sexual activities	30 (50.0)	37 (61.7)	67 (55.8)
Social activities	48 (80.0)	49 (81.7)	97 (80.8)

[Table 1. Self-experience of symptoms and impacts]

P0330

PREVALENCE OF ANTI-ANISAKIS SIMPLEX ANTIBODIES IN A COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN NORWAY: CORRELATION WITH DISEASE PHENOTYPE AND CLINICAL ACTIVITY

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Introduction: *Anisakis simplex* (AS) is a nematode parasite that can invade the stomach wall or the intestine in humans. Some previous studies have shown a high prevalence of anti-*Anisakis simplex* specific antibodies in in-

flammatory bowel disease (IBD). However, the clinical significance of this finding is uncertain. In addition, there is scarce data on the prevalence of AS infection in IBD in Nordic European countries.

Our objective is to characterize a large Norwegian IBD population for the presence of antibodies against AS and to correlate it with clinical features and disease activity.

Aims & Methods: In total, 157 IBD patients (88 Ulcerative Colitis-UC; 69 Crohn's disease-CD) and 42 matched healthy controls (H) were prospectively included from our IBD biobank. Demographic characteristics, Montreal phenotype classification and clinical activity (CRP, f-calprotectin and standard clinical and endoscopic indexes) were analyzed. Anti-AS antibodies including total immunoglobulins (IgS), IgG, IgM, IgA and IgE, were measured by ELISA test against larval crude extract as described in our previous study (1). Values higher than the mean of the optical density (OD) plus 2 standard deviation of the control group (H) were considered positive. GraphPad Prism version 8.4.2 was used for analysis and a p-value ≤ 0.05 was considered statistically significant.

Results: Of the 88 patients with UC (mean age 38,49 $\pm$ 15,07; 47% women), 26,5% had proctitis (E1 Montreal), 49,4% left-side colitis (E2) and 24,1% total colitis (E3). Sixty-nine patients with CD were studied (mean age 35,30 $\pm$ 12,64; 68% women). Of these, 15,5% had ileal affection (L1 Montreal), 32,8% colonic (L2) and 51,7 % ileocolonic CD (L3).

Total IgS OD mean values were 0,433 $\pm$ 0,115; 0,449 $\pm$ 0,134 and 0,476 $\pm$ 0,160 for H, UC and CD respectively; statistically significant for H vs CD only (p=0.025). IgG OD mean values were 0,555 $\pm$ 0,283; 0,469 $\pm$ 0,233 and 0,565 $\pm$ 0,247 for H, UC and CD respectively, only significant for H vs UC (p=0.041). IgM mean OD values were 1,691 $\pm$ 0,283; 1,740 $\pm$ 0,213 and 1,813 $\pm$ 0,186 for H, UC and CD respectively, statistically significant for H vs CD (p=0.035). IgA OD mean values were 0,883 $\pm$ 0,308; 0,933 $\pm$ 0,406 and 1,042 $\pm$ 0,514 for H, UC and CD respectively, which was significant for both H vs UC (p=0.05) and for H vs CD (p<0.001). We found no differences in IgE level between groups with mean OD values of 0,180 $\pm$ 0,081, 0,161 $\pm$ 0,070 and 0,170 $\pm$ 0,073 for H, UC and CD, respectively. The positivity rates in H, UC and CD for the different immunoglobulins are presented in Table1.

Group	Total IgS	IgG	IgM	IgA	IgE
	N (O.D $\geq$ 0,650)	N (O.D $\geq$ 1,000)	N (O.D $\geq$ 2,250)	N (O.D $\geq$ 1,500)	N (O.D $\geq$ 0,350)
H	3/43 (7%)	2/43 (4,6%)	0/43 (0%)	2/43 (4,6%)	1/43 (2,3%)
UC	7/84 (8,3%)	3/84 (0%)	0/84 (0%)	12/84 (14,3%)	1/84 (1,2%)
CD	11/70 (15,7%)	3/70 (4,3%)	0/70 (0%)	13/70 (18,6%)	1/70 (1,4%)

[Percentages of positive results for *Anisakis simplex* for the different Ig specific subsets in healthy, Ulcerative Colitis and Crohn's disease patients]

The group positive for IgA against AS was characterized by higher prevalence of total colitis (E3) in UC (87,5% vs 54,3%) and more ileocolonic forms (L3) in CD (44,4% vs 20,7%), and less disease activity as measured by CRP in both UC and CD.

Conclusion: Crohn's disease patients have a higher prevalence of anti-*Anisakis simplex* antibodies than healthy controls as measured by total IgS, IgM and IgA specific antibody levels. AS positive IBD patients tend to have more colonic involvement. These findings should be further studied since they could have relevant implications for clinicians as to consider testing for AS before starting immunosuppressive therapies in a subset of IBD patients.

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P0331

MACROPHAGES AS AN EMERGING SOURCE OF NOTCH LIGANDS: RELEVANCE IN CROHN'S DISEASE COMPLICATIONS

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Introduction: Fibrosis constitute the main complications associated to Crohn's disease (CD). Notch signalling has been implicated in lung, kidney, liver and cardiac fibrosis. Macrophages contribute to fibrosis through the release of different mediators and the pattern of secretion may vary according to their microenvironment.

Aims & Methods: The aim of the present study is to analyze the role of Notch ligands derived from macrophages in the complications of Crohn's disease (CD). With this purpose, we have analyzed: the expression of macrophages markers, cytokines, Notch ligands and fibrosis markers in patients with fistulizing and stenting pattern, the expression of macrophage markers and Notch ligands in macrophages treated with the main cytokines present in CD patients. Surgical resections from CD patients were categorized according to Montreal classification (B2 or B3) and unaffected ileal mucosa of patients with right colon cancer was used as control. mRNA levels of macrophages markers, Notch ligands, cytokines and fibrosis markers were analyzed in intestinal samples by RT-PCR. The expression of macrophage markers and Notch ligands were analyzed in IFN γ -U937, IL10-U937 and IL4-U937 treated cells. Results are expressed as fold induction (mean $\pm$ SEM, n $\geq$ 5). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test. Correlations were analyzed with the Spearman coefficient.

Results: The mRNA expression of *IFN γ* , *IL10*, and *IL4* was significantly higher in intestinal samples from B2 and B3 CD patients (19.3 $\pm$ 3.9, 6.7 $\pm$ 2.0, 20.7 $\pm$ 4.2, respectively for B3, and 9.8 $\pm$ 2.3, 4.3 $\pm$ 0.9, 17.9 $\pm$ 4.3, respectively for B2) than in controls (2.1 $\pm$ 0.3, 1.6 $\pm$ 0.3, 2.2 $\pm$ 0.5, respectively). The mRNA expression of *DLL3* and *DLL4* was significantly higher in intestinal samples from B2 (6.1 $\pm$ 1.3 and 9.3 $\pm$ 2.4, respectively) than in B3 CD patients (4.4 $\pm$ 1.0 and 1.8 $\pm$ 0.7, respectively) and in controls (0.9 $\pm$ 0.2 and 0.7 $\pm$ 1.2 respectively). The *DLL3* expression correlates positive and significantly with the expression of some fibrosis markers in B2 patients (*VIMENTIN* $r = 0.45$ $P = 0.03^*$, *FSP1* $r = 0.3$ $P = 0.01^*$, *SNAIL1* $r = 0.4$ $P = 0.01^*$, *SNAIL2* $r = 0.3$ $P = 0.01^*$ and *ZEB2* $r = 0.4$ $P = 0.02^*$). IFN γ -U937 treated cells increased significantly the mRNA expression of *DLL3* and *DLL4* (2.7 $\pm$ 0.7 and 2.6 $\pm$ 0.6, respectively) respect vehicle, while IL10-U937 treated cells increased only significantly the mRNA expression of *DLL3* (3.6 $\pm$ 1.3) respect vehicle and IL4-U937 treated cells increased the mRNA expression of *JAG1* (5.2 $\pm$ 1.8) respect vehicle.

Conclusion: Macrophages may act as a source of Notch ligands who could act as fibrosis mediators in CD patients with a stenting (B2) behavior. The microenvironment rich in IL10 and IFN γ could activate the process by favoring the expression of *DLL3* in macrophages.

Disclosure: Nothing to disclose

P0332

JANUS KINASE SELECTIVITY AND THE IMPACT ON CYTOKINE SIGNALING INHIBITION AT CLINICAL RHEUMATOID ARTHRITIS DOSES

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Introduction: Despite similar efficacy, in vitro studies have shown differences in JAK selectivity profiles for JAK inhibitors (JAKi) baricitinib (BAR), tofacitinib (TOF), and upadacitinib (UPA).¹ For example, BAR and UPA are JAK1/2 selective, while TOF is JAK1/3 selective, but each JAKi has activity against other JAKs. As JAKs form signaling pairs, differences in selectivity can lead to distinct pharmacologic profiles that may impact efficacy and safety.

To understand the basis of potential differences at therapeutic doses, we compared the selectivity and potency of filgotinib (FIL) and its major metabolite (MET) to those of BAR, TOF, and UPA in cytokine-stimulated peripheral blood mononuclear cells (PBMCs) and whole blood (WB).

Aims & Methods: PBMCs and WB from healthy donors were incubated in vitro with 8 doses of each JAKi, and levels of signal transducer and activator of transcription phosphorylation (pSTAT) were measured post-cytokine stimulation. Half maximal inhibitory concentration (IC₅₀) values were calculated in phenotypically sorted leukocyte populations by flow cytometry. Therapeutic dose relevance of the in vitro analyses was assessed using mean concentration-time profiles from JAKi pharmacokinetic data in RA subjects. For each JAKi, the time above IC₅₀ and average daily pSTAT inhibition were calculated for each cytokine/STAT pair in B cells, CD4+ T cells, CD8+ T cells, monocytes, and/or natural killer cells.

Results: PBMC and WB assays showed dose-dependent inhibition of cytokine-induced pSTATs with all JAKi (correlation between protein-adjusted IC₅₀ values from PBMCs and WB IC₅₀ values, $r^2=0.98$). Among the most potently inhibited pathways were the JAK1/TYK2-dependent cytokine, interferon alpha (IFN α), and the JAK1/2-dependent cytokine, interleukin (IL)-6. FIL and MET had weaker potencies against JAK2/TYK2 (G-CSF/pSTAT3), JAK1/2 (IFN γ /pSTAT1), and JAK2/2 (granulocyte-macrophage colony-stimulating factor [GM-CSF]-dependent pathways compared to JAK1/TYK2 (IFN α /pSTAT5). FIL/MET showed the highest selectivity for the JAK2/2 pathway (GM-CSF/pSTAT5) in monocytes.

The mean concentration-time profiles and time above IC₅₀ in 24h for each cytokine/STAT pathway showed that JAK1/2 (IL-6/pSTAT1) and JAK1/TYK2 (IFN α /pSTAT5) pathways were strongly modulated with all JAKi. FIL (200mg) showed similar activity in average target coverage and time above IC₅₀ to TOF (5mg) and UPA (15mg); conversely, FIL had reduced mean average inhibition and time above IC₅₀ levels against JAK1/2 (IFN γ /pSTAT1), JAK1/3-dependent cytokines (IL-2, -4, and -15), JAK2/TYK2 (G-CSF/pSTAT3), and JAK2/2 (GM-CSF/pSTAT5)-dependent pathways compared to TOF and UPA, and, in certain cases to BAR.

Conclusion: Different JAKi modulate distinct cytokine pathways to varying degrees, and no agent potently and continuously inhibited an individual cytokine pathway throughout the dosing interval. FIL (200mg) showed a similar profile to TOF, BAR, and UPA against the JAK1/TYK2- (IFN α /pSTAT5) or JAK1/2-dependent (IL-6/pSTAT1) responses, consistent with the role of these pathways in clinical efficacy.²

However, FIL displayed a distinct pharmacologic profile from other JAKi, with reduced activity on JAK1/2 (IFN γ)-, JAK1/3 (IL-2, -4 and -15)-, JAK2/TYK2 (G-CSF)-, and JAK2/2 (GM-CSF)-dependent pathways, which play key roles in hematopoiesis and immune function. These data suggest that FIL (200mg) may have less impact on certain immune functions signaling via JAK2 and JAK3 than those of the approved doses of TOF, UPA, and BAR.

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Disclosure: AC, PG-T, BM, FC, AM and JDP: Gilead Sciences, Inc.

P0333 WITHDRAWN

P0334

DSS COLITIS IS WORSENERED AND PROLONGED IN GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR KNOCK OUT MICE COMPARED TO WILD TYPE MICE

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Introduction: Glucagon-like peptide-1 (GLP-1) is secreted from the enteroendocrine L-cells in both the small intestine and colon. GLP-1 is an anti-diabetic hormone but has been associated with both intestinal growth and systemic inflammatory activity in recent years. Research has shown that intestinal injury increases GLP-1 secretion in experimental animals [1]. GLP-1 has also been shown to ameliorate acute small intestinal injury such as chemotherapy-induced mucositis [1]. Furthermore, depletion of the GLP-1 secreting L-cells abolished recovery in a model of small intestinal injury [2]. We hypothesized that GLP-1 receptor signaling is crucial for recovery from dextran sulfate sodium (DSS)-induced colitis in mice.

Aims & Methods: We aimed to investigate the course of DSS colitis in mice lacking GLP-1 receptor signaling. The constitutive KO mouse for GLP-1R (GLP-1R KO) was generated by deleting exons 4 and 5 of the GLP-1R gene upon Cre expression [3]. Mice were bred by heterozygote crossing, and wild type (WT) littermates served as controls. A total of 34 mice (aged 12-13 weeks) were randomized into two groups, one group was given 3% DSS in drinking water, the other group was given normal drinking water for 8 days, and after all mice received normal drinking water. Body weight (BW) was monitored from day 3 until termination on day 13. Two hours before euthanasia, mice received a bolus of 4-kDa FITC dextran (600 mg/kg) by oral gavage for determination of intestinal permeability. Blood was drawn and the amount of FITC in plasma was evaluated by spectrophotometry. Small intestines and colon were removed, flushed carefully with saline and weighed. Tissue from duodenum, jejunum, ileum and colon were analyzed for content of myeloperoxidase (MPO). Ear snips were genotyped by polymerase chain reaction, revealing n=7 in the DSS-GLP-1R KO group, n=6 in the DSS-WT group, the water-GLP-1R KO group and the water-WT group. Heterozygotes were excluded. Percentage body weight (BW) loss over time was analyzed with two way ANOVA. MPO activity, FITC in plasma and intestinal parameters were analyzed with one-way ANOVA. Sidak's multiple comparisons test were used to test for differences between DSS-GLP-1R KO and DSS-WT.

Results: DSS-WT mice had a maximum of 5.9 (±2.2) % loss in BW occurring at day 10, however, BW was fully recovered at day 13 (0.4 (±2.0) %) in DSS-WT mice. Contrary to this the DSS-GLP-1R KO mice had a severe BW loss at day 11 (13.2 (±3.3) %) and did not recover at day 13 (10.5 (±2.8) %, p< 0.01). Myeloperoxidase activity was increased in colonic tissue in DSS-GLP-1R KO compared to DSS-WT (3.6 (±0.7) vs. 2.1 (±0.4) U/mg, p< 0.05). No differences were found in FITC and intestinal weights between any of the groups.

Conclusion: GLP-1 receptor signaling is crucial for recovery from DSS colitis.

	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 13
Group	BW loss % (±SEM)	BW loss % (±SEM)	BW loss % (±SEM)	BW loss % (±SEM)	BW loss % (±SEM)	BW loss % (±SEM)	BW loss % (±SEM)	Colon MPO U/mg (±SEM)
DSS-WT	5.6 (1.6)	5.7 (1.8)	5.8 (2.1)	5.9 (2.2)	4.6 (2.0)	1.5 (1.5)	0.4 (2.0)	2.1 (0.4)
DSS-GLP-1R KO	1.7 (1.3)	6.0 (2.0)	9.3 (2.2)	11.8 (3.0)	13.2 (3.3)*	11.4 (4.4)*	10.5 (2.8)**	3.6 (0.7)*
Water-WT	0.8 (0.8)	0.7 (1.3)	0.1 (1.0)	0.6 (1.0)	0.5 (1.0)	2.1 (0.8)	1.4 (0.6)	0.1 (0.0)
Water-GLP-1R KO	0.5 (0.5)	0.4 (0.8)	0.5 (1.1)	1.2 (0.6)	0.2 (1.1)	1.7 (1.5)	0.5 (0.6)	0.3 (0.2)

[Table 1. BW loss in percentage from day 3 after DSS and MPO activity in colonic tissue at day 13. * = p<0.05 and ** = p<0.01 compared to DSS-WT (Sidak's)]

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P0335

DIET-INDUCED REMISSION IS NOT LINKED TO BILE ACID MODIFICATION

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Introduction: Nutritional therapy plays a central role in the treatment of Pediatric Crohn's Disease (pedCD)[1]. The Crohn's Disease Exclusion Diet (CDED) is better tolerated and able to sustain remission better than Exclusive Enteral Nutrition (EEN) in pedCD [2]. Microbiome changes are strongly associated with the therapeutic effect.[2] Bile acids (BA) have been shown to play a central role in modulating intestinal immune response and it is known that their composition can be altered by changes in the gut bacterial community [3-5]. A decreased secondary BA (secBA) and increased primary BA (priBA) profile characterizes IBD patients from healthy controls. In pedCD, a specific primary BA signature was recently described in children who do not sustain remission after EEN [6], suggesting an important role for BA in the mechanism of nutritional therapy in pedCD.

Aims & Methods: We investigated changes in the fecal BA pool in stool samples from the CDED-RCT, a 12-week prospective trial comparing two different nutritional therapies (CDED+Partial EN vs EEN) for induction of remission in mild to moderate CD. After 6 weeks, the EEN group was al-

lowed to return to free diet with 25% of calories from PEN. Endpoints of the study were intention to treat (ITT) remission at week 6 (defined by Pediatric Crohn's Disease Activity Index (PCDAI) < 10) and corticosteroid-free ITT sustained remission at week 12. Stool samples were collected at week (W)0, W3, W6 and W12. Primary, secondary and total BA concentrations of 94 samples at different timepoints were measured by Liquid Chromatography coupled to Mass Spectrometry and analyzed according to clinical outcome groups of sustained remission, non-sustained remission and no-remission.

Results: There were no significant differences in PCDAI score, conjugated or unconjugated priBA, secBA or total BA concentration between CDED and EEN samples at baseline. In this subgroup of the previously reported CDED-RCT[2], CDED induced remission in 13 out of 15 patients at week 6 (n=13, 9, 15, 8 at W0, W3, W6, W12, respectively), which was maintained in 7 out of 8 patients at week 12; in the EEN group 10 out of 13 patients achieved remission at week 6 (n=12, 11, 13, 12 at W0, W3, W6, W12) and 6 out of 12 patients maintained remission until week 12. CDED did not induce changes in the concentration of conjugated or unconjugated priBA, secBA or in total BA in all time points investigated. In contrast, EEN samples showed a significant decrease in priBA concentration at W6 and W12 compared to CDED samples.

Conclusion: Diet-induced remission is not associated with bile acid modification. Although CDED was shown to be more effective in achieving sustained remission than EEN, no significant differences in BA composition were found in CDED fecal samples at different timepoints. Further studies on microbiome or other metabolites are warranted to explore the mechanism of diet-induced remission.

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Disclosure: Nothing to disclose

P0336

SACCHAROMYCES CEREVISIAE, CANDIDA ALBICANS AND ADHERENT-INVASIVE ESCHERICHIA COLI (AIEC) INTESTINAL COLONIZATION IS NOT ASSOCIATED WITH ASCA DETECTION IN CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is a multi-factorial disorder and familial aggregation of CD has long been recognized. Anti-Saccharomyces cerevisiae antibodies (ASCA) are present in 50-60% of patients with CD but also, for unknown reasons, in 20-25% of their healthy relatives (HR), while solely 0-5% of controls. Culture based methods revealed that CD patients and their first-degree relatives are more frequently and more heavily colonized by *Candida albicans* than are controls while high prevalence of adherent-invasive *Escherichia coli* (AIEC) was reported in the intestinal mucosa of CD patients.

Aims & Methods: The aims of the present study were to evaluate the presence of *C. albicans*, *S. cerevisiae* and AIEC in the digestive tract in CD patients, their first degree HR, and controls, and to correlate colonization by these microorganisms with ASCA detection.

We included 191 individuals comprising CD patients (CD; n=51), their first degree HR (HFDR; n=89) and matched healthy controls (HC; n=51). Faecal samples were collected and the microbiota composition, diversity and loads were assessed by 16S rRNA gene sequencing and quantitative PCR. Faecal *C. albicans* and *S. cerevisiae* carriage was evaluated by ITS sequencing. Adherent-Invasive *Escherichia coli* (AIEC) detection in stool samples and their respective phylotyping/invasiveness classification were evaluated. Other CD-associated biomarkers (serum IgG and IgA ASCA and faecal calprotectin) were assessed.

Results: Mycobiome analysis revealed significant differences between fungal communities in adult versus paediatric individuals and this difference was independent of CD status of the patient, disease location and levels of calprotectin. Carriage of *C. albicans* was more frequent in adult than in paediatric patients (P=0,02). Conversely, carriage of *S. cerevisiae*

was more frequent in paediatric than in adults individuals ($P=0.04$). Analysis of CD biomarkers showed that levels of serum ASCA IgG were significantly higher in patients with CD than in HFDR ($P=0.0001$) and controls ($P=0.0001$). ASCA status was not correlated with carriage of *S. cerevisiae*, *C. albicans* or AIEC in both CD patients and their HR. No dominant genera was evidenced when considering disease status or disease location.

Conclusion: Our study confirms the presence of specific features in adult versus paediatric mycobiome independently of the disease status. The presence of ASCA was not correlated to the carriage of *S. cerevisiae*, *C. albicans* or AIEC strains in the gut of patients with CD.

Disclosure: Nothing to disclose

P0337

SUCNR1 DEFICIENCY IMPAIRS INFLAMMASOME ACTIVATION AND AMELIORATES CHRONIC DSS COLITIS

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Introduction: Crohn's Disease (CD) is a chronic pathology characterized by a persistent inflammation. Nlrp3 inflammasome is a critical regulator of intestinal homeostasis but its role in CD is still controversial. We have recently reported that SUCNR1 mediates intestinal inflammation and fibrosis.

Aims & Methods: We aim to analyze the role of SUCNR1 in inflammasome activation and in chronic DSS-colitis. In wild-type (WT) and SUCNR1-/- mice chronic DSS-colitis was induced with four cycles with DSS (7 days) separated by 10 days without DSS. Intestinal resections from CD and non-IBD patients were obtained. The expression of inflammatory, inflammasome and pro-fibrotic markers was analyzed by qPCR and Western-Blot and the collagen layer with Sirius Red Staining. Results are expressed as fold induction (mean±SEM, n≥5). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test. Correlations were analyzed with the Spearman coefficient.

Results: DSS-treated-WT-mice showed: loss of body weight, reduction in colon length, increased expression of proinflammatory and profibrotic markers and a thicker collagen layer. DSS-treated-SUCNR1-/-mice exhibited: a lower loss of body weight, a reduced expression of proinflammatory and profibrotic markers and collagen layer. DSS-WT-mice showed increased protein levels of cleaved caspase-1 versus SUCNR1-/-mice. In CD patients, the expression of Nlrp3, IL18, Caspase1 and ASC were significantly increased compared with Non-IBD patients. Of interest, a positive and significant correlation was observed between the expression of SUCNR1 and Nlrp3 ($r_{\text{Spearman}}=0.4639$, $P=0.0033$), IL18 ($r_{\text{Spearman}}=0.3716$, $P=0.0018$), Caspase1 ($r_{\text{Spearman}}=0.5621$, $P=0.0002$) and ASC ($r_{\text{Spearman}}=0.4754$, $P=0.0019$).

Conclusion: Lack of SUCNR1 ameliorates chronic DSS-Colitis and impairs inflammasome activation. In CD patients, the expression of inflammasome components is significantly increased. In addition, the expression of SUCNR1 positively correlates with the expression of the inflammasome components Nlrp3, IL18, Caspase1 and ASC. Hence, we suggest that SUCNR1 might be a promising pharmacological target for CD-treatment.

Disclosure: Nothing to disclose

P0338

PROFILING OF HUMAN CIRCULATING DENDRITIC CELLS AND MONOCYTES SUBSETS DISCRIMINATES TYPE AND MUCOSAL STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Intestinal dendritic cells (DC) and macrophages govern the mechanisms of immune homeostasis having a role in inflammatory bowel disease (IBD) onset. However, the profile of their circulating precursors (DC and monocytes) in IBD has not been previously described in depth.

Aims & Methods: Our aim was to characterize blood DC and monocyte subsets in healthy controls (HC) and IBD patients in order to understand their potential implication in IBD pathogenesis. 18 HC and 64 IBD patients were recruited. IBD patients were categorized into Crohn's disease (CD) and ulcerative colitis (UC), either endoscopically active (aCD and aUC) or quiescent (qCD and qUC), based on the SES-CD or the Mayo index endoscopic subscore. Blood circulating type 1 conventional DC (cDC1), type 2 conventional DC (cDC2), plasmacytoid DC (pDC), classical monocytes, non-classical monocytes and intermediate monocytes were identified by flow cytometry and characterized for the expression of 18 homing and activation markers ($\beta 7$, CCR1, CCR2, CCR3, CCR5, CCR6, CCR7, CCR9, CCRL1, CD40, CD86, CD137L, CD274 (PD-L1), CLA, CXCR1, CXCR3, ICOSL, HLA-DR). Association between markers and the presence, type or activity of IBD was tested by logistic regression. Discriminant canonical analysis were also performed to classify the patients on their own endoscopy category.

Results: All groups (HC, aCD, qCD, aUC and qUC) were separated from the others based on the discriminant canonical analyses of the 18 markers applied over all DC and monocytes subsets. Specifically, CCRL1, CCR3 and CCR5 expression on cDC1, CCRL1 on non-classical monocytes and CCR9 and $\beta 7$ on classical monocytes were highly associated to IBD. CCR3 displayed an odds ratio (OR) of 2.29 along with its 95% confidential interval (CI) between 1.11 and 4.75, showing a strong association with activity in CD; whereas the other markers displayed an inverse association with IBD. Hence, expression of CCRL1 on cDC1 and non-classical monocytes from aUC showed an OR (95% CI) of 0.23 (0.08-0.66) and 0.52 (0.28-0.95), respectively. In the case of qUC, CCR5 on cDC1 and $\beta 7$ on classical monocytes displayed an OR (95% CI) of 0.10 (0.01-0.83) and 0.56 (0.34-0.90), respectively. CCR9 was inversely associated to qCD with an OR (95% CI) of 0.64 (0.46-0.89) in the classical monocytes subset. Indeed, the same markers (excluding $\beta 7$) were also associated with IBD when all DC and monocyte subsets were considered at the same time.

Conclusion: Differences on the expression of migration markers CCR3, CCR5, CCR9, $\beta 7$ and decoy receptor CCRL1 on circulating DC and monocyte subsets from IBD groups suggest the presence of constitutive migratory differences underlying IBD pathogenesis in CD or UC and its condition (inflamed or non-inflamed).

Disclosure: Nothing to disclose

P0339

SUCCINATE RECEPTOR MEDIATES LEUKOCYTE-ENDOTHELIAL CELL INTERACTIONS INDUCED BY TNF α

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Introduction: Inflammation is associated with significant metabolic changes that promote the accumulation of the Krebs cycle intermediate succinate, and this metabolite seems to contribute to inflammatory conditions like arthritis and colitis through the activation of its receptor SUCNR1.

Aims & Methods: The aim of the present study is to analyze whether the succinate-SUCNR1 pathway contributes to the leukocyte-endothelial cell interactions that initiate the inflammatory response.

We evaluated leukocyte rolling and adhesion, a) in vivo, by intravital microscopy in cremaster venules of wild-type (WT) and SUCNR1^{-/-} mice treated with TNF α (500 ng/mice i.p., 4h), and with succinate (1 mM) or its vehicle intraescrotally; and b) in vitro, by analyzing the interactions of human mononuclear leukocytes (PBMCs) with endothelial cells (HUVEC treated with succinate 1mM and TNF α 20ng/ml, or their vehicles) in a flow-chamber. HUVECs and PBMCs were isolated from healthy donors. Results are expressed as mean $\pm$ SEM (n $\geq$ 5) and analyzed by ANOVA + Newman-Keuls test.

Results: The increase in leukocyte-endothelial cell interactions induced by TNF α in WT mice were not affected by the local injection of succinate. However, a reduced response to TNF α was observed in mice lacking SUCNR1 and treated with succinate or its vehicle (Table 1).

	WT	SUCNR1 ^{-/-}		
	Vehicle	Succinate	Vehicle	Succinate
Rolling	742 $\pm$ 267	775 $\pm$ 101	175 $\pm$ 35*	192 $\pm$ 49*
Adhesion	405 $\pm$ 108	417 $\pm$ 104	198 $\pm$ 18*	269 $\pm$ 40*

[Table 1. (Data expressed as % vs control conditions (WT mice injected with vehicle i.p. and intraescrotally); p<0.05 vs respective WT group).]

In vitro, succinate tended to increase PBMC rolling and adhesion (Rolling:146 $\pm$ 28%, Adhesion:212 $\pm$ 32% vs control) but did not affect the interactions stimulated by TNF α (Rolling:98 $\pm$ 22%, Adhesion:99 $\pm$ 41% vs TNF α).

Conclusion: Our results suggest that the endogenous release and accumulation of succinate observed in numerous inflammatory diseases may contribute to inflammation by promoting leukocyte-endothelial cell interactions.

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Disclosure: Nothing to disclose

P0340

STUDYING THE FEATURES OF ANEMIA IN INFLAMMATORY BOWEL DISEASES AND ITS RELATIONSHIP WITH SOME MARKERS OF DYSFUNCTION

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Introduction: Anemia is one of the most common manifestations of extraintestinal manifestations of Crohn's disease (CD) and ulcerative colitis (UC). The incidence of anemia in all patients with inflammatory bowel disease (IBD) varies from 16% of outpatients to 68% of hospitalized patients. According to modern concepts, the main role in the development of IBD is played by immune disorders with dysregulation of cytokines. The further development of inflammatory reactions is facilitated by a violation of the barrier function of the intestine, mucus formation, metabolic and regulatory impairment, and chronic intoxication. The role of endothelial dysfunction (ED) in the pathogenesis of IBD associated with anemia remains the least studied.

Aims & Methods: Aim: to identify the incidence of anemia in patients with IBD and its relationship with some markers of ED.

Methods: In the period from August 2015 to December 2019, 449 patients with IBD were examined. In all subjects were determined a total blood count with reticulocytes counting, homocysteine content, highly sensitive C-reactive protein (h/s-CRP), iron, ferritin, iron saturation index, vitamin D and platelet count in the blood, albumin in urine, calprotectin and lactoferrin in feces. If necessary, the patient was repeated studies. The average age of patients was 35 $\pm$ 10.87. Of these, 248 were men and 201 were women (53 and 47%, respectively). The duration of the disease was 7.09 $\pm$ 8.06.

Results: In the total group of patients with IBD, out of 449 studies, a decrease in hemoglobin level was noted in 414 (92.2%), a decrease in hematocrit level in 401 (89.3%); a decrease in red blood cells in 278 (61.9%) and in 102 (22.7%) increase; in 258 (57.4%) cases a decrease in the level of reticulocytes and in 74 (16.4%) cases an increase; in 414 (92.2%) cases a decrease in the level of iron; in 322 (71.7%) cases a decrease in the level of ferritin and in 112 (24.9%) an increase; in 198 (44%) cases a change in the saturation index. In 369 (82.1%) cases there was an increased content of homocysteine in the blood, in 405 (90.2%) - the level of the h/s CRP, in 322 (71.7%) - thrombocytosis, in 411 (91.5%) - a decrease in the content of vitamin D, in 308 (68.6%) albumin in the urine was detected, and in 411 (91.5%) an increased content of fecal calprotectin was revealed, and in 431 (95.9%) an increase in lactoferrin in feces. In a separate analysis of the identification of each of these indicators in the UC and CD groups, no difference was revealed (p>0.05). A correlation was found between some indicators of ED, the severity of the clinical course and anemia in patients with IBD.

According to the results of the study, in 82.1% of patients with IBD against the background of developing anemia, a significant violation of the function of the vascular endothelium of various degrees was observed, as evidenced by an increased level of homocysteine. Although ED was equally common in patients with IBD, lower compensatory capabilities of vascular

endothelium were characteristic of patients with CD. A reliable relationship was also found between the indicators of ED and the severity of IBD, as well as the clinical and endoscopic activity of the process. The revealed violations confirm the hypothesis about the participation of ED in the pathogenesis of IBD.

Conclusion: Thus, damage to the vascular wall, closely associated with developing anemia, may be one of the pathogenetic mechanisms of IBD. Further study of this problem can be effective in terms of both improving the targeted treatment of IBD and the prevention of vascular pathologies in this group of patients.

Disclosure: Nothing to disclose

P0341

THE GUT MICROBIOME OF HEALTHY SIBLINGS OF INFLAMMATORY BOWEL DISEASE (IBD) TWINS DISPLAYS IBD SIGNATURES

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Introduction: Recent studies have associated IBD with shifts in the composition of the intestinal microbiome, but it is currently not clear whether these changes are *cause* or *consequence* of the disease. Also, the gut microbiome is known to be influenced by genetics and (early childhood) environment. We therefore studied the gut microbiome of IBD affected twin pairs, because healthy individuals with an IBD affected twin sibling are at risk of developing IBD, offering the unique opportunity to study the microbiome of individuals at increased risk for IBD, *before* IBD might develop.

Aims & Methods: Fecal samples were obtained from 99 twin-siblings belonging to 51 twin pairs (3 fecal samples did not pass quality control); 24 were from IBD-concordant and 75 from IBD-discordant twin pairs. From these 99 twin siblings 53 belonged to mono-, and 46 to dizygotic twin pairs. In addition, we studied 495 healthy age-, and sex-matched controls (twin siblings:controls = 1:5), and 99 self-reported IBD patients, from a population-based control cohort (the Dutch Microbiome Project). Whole-genome metagenomic shotgun sequencing was performed and microbial (on taxonomic and pathway level) and community diversity were compared between healthy twin siblings, IBD twin siblings, and healthy and IBD controls. Furthermore, multivariable boosted general linear model analyses were performed with as individual outcomes 241 individual species and 394 predicted bacterial pathways adjusted for age, sex, body mass index, antibiotics use, proton pump inhibitor use, disease location and IBD phenotype. A false discovery rate (FDR) adjusted p-value < 0.1 was used as cut-off value for statistical significance.

Results: No differences were found in species nor pathways between healthy twin-siblings and their mono- or dizygotic IBD twin siblings (FDR < 0.1). In addition, healthy twin siblings and their IBD twin siblings had a comparable overall taxonomical and functional composition (p=0.22,

p=0.72 respectively), however, the overall gut microbiome composition of healthy twin siblings was different from healthy controls (taxonomic: p=0.02, functional: p=0.0002). In IBD twin siblings and in healthy twin siblings, 44 species and 119 pathways and 22 species and 159 pathways, respectively, were found to be differentially abundant (FDR < 0.10), compared to healthy controls. Of these differentially abundant species and pathways, 10/44 (23%) of species, and 85/119 (71%) pathways were shared between IBD twin siblings and healthy twin siblings. Most of these shared species and pathways have previously been associated with IBD, e.g. an increase in the pathogenic species *Escherichia coli* and of pathways involved in production of adhesion related virulence mechanisms, and a decrease in the production of short chain fatty acids (SCFAs).

Conclusion: In this largest IBD twin microbiome study published so far, we found that the gut microbiome of healthy twin siblings, who are at increased risk of developing IBD, displays IBD-like signatures, both at a taxonomic and functional level, similar to the gut microbiome of their IBD-affected twin siblings. These IBD-like microbiome signatures might precede the onset of IBD and thus point towards a causal role of the gut microbiome in the pathogenesis of IBD.

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P0342

IMPACT OF ANTI-TNF- α AGENTS ON MACROPHAGES RESPONSE TO ADHERENT-INVASIVE *ESCHERICHIA COLI* INFECTION IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Anti-TNF- α agents are the most effective drugs but its mechanisms remain imperfectly understood. Macrophages from Crohn's Disease (CD) patients are defective to eliminate CD-associated adherent-invasive *E. coli* (AIEC). The effect of TNF- α inhibitors on macrophages behavior against AIEC has not been investigated so far in patients with CD. We aimed to (i) assess the impact of anti-TNF- α therapy on AIEC survival within macrophages, and (ii) evaluate the impact of anti-TNF- α therapy on macrophages proteome in response to AIEC infection in CD patients.

Aims & Methods: Peripheral blood monocyte-derived macrophages (MDM) were obtained from 44 CD patients including 22 with and 22 without anti-TNF- α treatment, 22 UC patients and 22 healthy volunteers (HV). MDM were infected with AIEC LF82 reference strain. The numbers of intracellular bacteria were determined at 6h post-infection. The "bottom-up" proteomic analysis of macrophages was performed at basal state and after 6h of AIEC LF82 infection, by mass spectrometer, using the *label-free* quantification. All the differentially expressed proteins (≥ 2 peptides) were selected with an ANOVA *p-value* ≤ 0.05 and a minimal fold change of 1.3.

Results: AIEC LF82 survival was significantly 3.7-fold lower in MDM from CD patients with anti-TNF- α treatment compared to those without anti-TNF- α treatment (*p*=0.006). Among the 1173 proteins identified by the proteomic analysis, 893 have a human origin and 250 a bacterial origin. The principal component analysis highlighted a relevant impact of AIEC LF82 infection with 23.9% of macrophages proteome affected, regardless of the MDM origin (*p*< 0.05). The relative abundance of macrophages proteins following AIEC infection was significantly decreased within MDM from CD patients compared to HV. Four proteins were specifically dysregulated in MDM from CD patients treated with anti-TNF- α , following AIEC exposure: CD82 (*p*=0.007), ILF3 (Interleukin enhancer-binding factor 3) (*p*=0.001), FLOT1 (Flotillin-1) (*p*=0.007) and CHI3L1 (Chitinase-3-like protein 1) (*p*=0.035). Three of them, CD82 (*p*=0.05), ILF3 (*p*=0.008) and CHI3L1 (*p*=0.02) were already dysregulated at basal state in CD patients treated with anti-TNF- α therapy.

Conclusion: Anti-TNF- α agents are able to restrict AIEC bacterial replication within macrophages from CD patients. Our proteomic analysis revealed four proteins (CD82, ILF3, CHI3L1 and FLOT1) that could explain a such impact and could be potential therapeutic targets in CD.

Disclosure: Nothing to disclose

P0343

MICROBIAL REGULATION OF EPITHELIAL HEXOKINASE 2 LINKS MITOCHONDRIAL METABOLISM AND CELL DEATH IN COLITIS

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Introduction: Hexokinases (HK) are a family of five isoenzymes, which catalyze the first step of glycolysis and thereby limit its pace. HK2 is considered the prototypic inducible isoform of all HK family members as it can be stimulated by various environmental or proinflammatory factors and is upregulated during inflammation and ulcerative colitis [1-3]. Furthermore, in addition to its metabolic function, HK2 functions as an innate immune receptor for bacterial cell wall components in myeloid cells [4].

Aims & Methods: Our aim was to examine the function of HK2 for host-microbiota-interactions and intestinal inflammation. To that end, we generated transgenic mice lacking *Hk2* specifically in intestinal epithelial cells (*Hk2*-ΔIEC), tested their susceptibility to acute inflammation using the dextran sodium sulfate (DSS) colitis model and isolated IECs for RNA-sequencing to identify functions and pathways altered by loss of *Hk2*. We then generated a *Hk2*-deficient ($\Delta Hk2$)Caco-2 cell line using CRISPR-Cas9 and intestinal organoids from *Hk2*-ΔIEC mice to functionally validate findings from our RNA-seq data involved in HK2-mediated signaling during inflammation. In parallel, we stimulated intestinal epithelial cell lines and gnotobiotic mice with bacterial strains and metabolites to identify microbial agents that modulate *Hk2* expression. Ultimately, we tested whether supplementing these microbial metabolites alters colitis outcome *in vivo* through modulation of HK2.

Results: *Hk2*-ΔIEC mice were less susceptible to acute DSS colitis evident by less intestinal inflammation and weight loss. RNA-sequencing of IECs from *Hk2*-ΔIEC mice during acute colitis revealed upregulation of type I and II interferon signaling and downregulation of pro-apoptotic signaling dependent on loss of *Hk2*. *Hk2*-ΔIEC mice exhibited reduced numbers of apoptotic cells compared to their WT littermates. Proinflammatory stimulation of $\Delta Hk2$ Caco-2 cells and intestinal organoids also showed a protection from cell death apparent from lower levels of cleaved Caspase 3 and cleaved Poly(ADP-Ribose)-Polymerase 1 (PARP1). Using $\Delta Hk2$ Caco-2 cells we identified disrupted mitochondrial function and reduced levels of peptidylprolyl isomerase f (*Ppiif*) as a result of loss of HK2 potentially leading to the repression of pro-apoptotic signaling during intestinal inflammation. Additionally, we found that the intestinal microbiota strongly regulated HK2 expression and activity. We identified individual bacteria and microbial metabolites, which modulate *Hk2* expression both in gnotobiotic mice and epithelial cell lines. Specifically, the short-chain fatty acid

butyrate was a potent repressor of *Hk2* and *Ppif* expression *in vitro* and *in vivo* and, most important, oral supplementation protected WT but not *Hk2*-ΔIEC mice from DSS colitis indicating a *Hk2*-dependent mechanism.

Conclusion: We identified the microbiome as a central regulator of HK2 and cell death in the intestinal epithelium. The microbial metabolite butyrate could therefore act as a potential therapeutic approach to ameliorate colitis by downregulation of HK2.

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Disclosure: Nothing to disclose

P0344

DEGREE OF HISTOLOGICAL ACTIVITY IS NOT ASSOCIATED WITH VEDOLIZUMAB THERAPY OUTCOME IN ULCERATIVE COLITIS

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Introduction: Histological inflammation is known to be associated with increased risk of disease relapse in patients with ulcerative colitis (UC). Vedolizumab (VDZ) is a gut selective anti-integrin which inhibits intestinal immune cell-trafficking. Whether the degree of histological activity at the time of VDZ therapy initiation is associated with therapy outcome is not known. We aimed to determine if there is an association between histological activity at the time of VDZ initiation and outcome of therapy.

Aims & Methods: A retrospective review was performed to identify UC patients treated with VDZ who had undergone an endoscopic assessment prior to therapy commencement. Baseline demographic data, information on therapy outcome and Mayo endoscopic sub score (MES) was collected for all patients. Endoscopic biopsies were retrieved and were scored for histological activity using the Geboes Score (GS). For Kaplan Meir analyses of primary endpoint, the cohort was dichotomised around a GS grade of 5. Primary endpoint was VDZ therapy outcome defined as persistence on VDZ therapy over time. Secondary endpoints included association between GS and MES and the association between a combined endoscopic and histological endpoint (MES = 3 & GS grade 5) and VDZ therapy outcome.

Results: N=33 patients were included [median age 44.3 years (range 17.2-84.3); 36% male gender]. 24%, 43% and 33% of the cohort had proctitis, left-sided colitis and extensive colitis respectively. 67% of subjects had prior anti-TNF exposure. Median time from endoscopy to commencement of VDZ was 9 weeks. Median study follow-up was 68 weeks (range 6.1-228.7). 3%, 21%, 42% and 33% had MES of 0, 1, 2 and 3 respectively. GS grade was significantly associated with MES ($p = 0.04$). GS grade was not associated with time to discontinuation of VDZ ($p = 0.64$). Combined endoscopic and histological endpoint was not associated with time to discontinuation of VDZ ($p = 0.43$). The presence of lamina propria eosinophils was not associated with time to discontinuation of VDZ ($p = 0.92$).

Conclusion: GS grade is associated significantly with MES which has been demonstrated previously. Neither histological activity alone nor in combination endoscopic activity were associated with outcome of VDZ therapy. Assessment of histological activity does not appear to provide additional information when selecting patients for VDZ therapy.

Disclosure: Nothing to disclose

P0345

WNT1-INDUCIBLE SIGNALING PROTEIN-1 IS ASSOCIATED WITH INTESTINAL FIBROSIS IN CROHN'S DISEASE

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Introduction: Intestinal fibrosis in Crohn's diseases is characterized by a progressive and excessive deposition of extracellular matrix components. The exact pathomechanism leading to fibrosis is still incompletely understood and no specific anti-fibrotic therapy is available.

Aims & Methods: We have recently shown, that specific Wnt-signals, such as the WNT1-inducible signaling protein-1 (WISP1), are involved in regulation of intestinal inflammation and wound healing. Since they have been associated with fibrosis formation in other organs, we now investigated their implications in fibrosis formation in the gut.

Using a qPCR based microarray a total of 84 different genes associated with Wnt-signaling were analysed in a primary analysis of paired samples (fibrosis vs. control) of patients with Crohn's disease. For verification of the results surgical specimen of 32 patients with Crohn's disease were examined using qPCR. For all samples a histological score was applied to quantify fibrosis formation. mRNA expression was then correlated to fibrosis severity using Spearman Correlation. For further analysis of cell function during fibrosis, Crohn's associated primary fibroblasts from a fibrotic section (Crohn group) and non-inflammatory, non-fibrotic section (control group) were isolated. Cell motility was monitored by wound healing assays. Cell proliferation was measured by Ki-67 staining. Protein expression such as WISP1, β-catenin and phospho-β-catenin were evaluated by Western blot.

Results: Using microarray analysis a definite set of Wnt-signaling components showed significant upregulation during fibrosis in Crohn's disease: the mRNA levels of LEF1, SFRP4, WNT2, WNT3A, WNT8A were increased in the fibrotic tissue. Interestingly, our results showed that WISP1 was 2x fold upregulated compared to control non-fibrotic tissue. This upregulation was validated through qPCR using surgical specimen of fibrotic Crohn's disease. A moderate agreement between the fibrotic score and pathological classification was observed ($p = 0.587$). Primary fibroblasts isolated from intestinal tissue of Crohn disease patients were consistently α-SMA and vimentin positive. While there was no statistical difference in proliferation between the control group and Crohn group after 6 hours and 12 hours, a significant difference in cell proliferation after 24 hours was detected. Wound healing assays showed that the healing rate in the Crohn group were significantly faster after 24 hours ($P < 0.01$). Western blot result showed that the expression of β-catenin protein in the Crohn group was significantly increased ($p = 0.0453$).

Conclusion: Our study thus identifies activation of Wnt/ β-Catenin and especially WISP1 signals during fibrosis formation in Crohn's disease. We now aim to further characterize the role of WISP1 during this process. Antibodies against WISP1 might be a potential therapeutic target for attenuation of intestinal fibrosis in Crohn's disease.

Disclosure: Nothing to disclose

P0346

ROLE OF IFN γ -ACTIVATED MACROPHAGES IN THE EPITHELIAL MESENCHYMAL TRANSITION IN CROHN'S DISEASE

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Introduction: Macrophages contribute to fibrosis through the release of different mediators (like wnt ligands or TGF β) and the pattern of secretion may vary according to their phenotype, which in turn depends on the microenvironment.

Aims & Methods: The aim of the present study is to analyze the role of IFN γ in the complications of Crohn's disease (CD). With this purpose, we have analyzed: the expression of IFN γ in patients with fistulizing and stenting pattern, the role of IFN γ in the expression of macrophage markers, wnt ligands and TGF β in macrophages, the expression of epithelial mesenchymal transition (EMT) markers in epithelial colonic cells co-cultured with IFN-treated macrophages. Surgical resections from CD patients were categorized according to Montreal classification (B2 or B3) and unaffected ileal mucosa of patients with colon cancer was used as control. mRNA and protein IFN γ levels were analyzed in intestinal samples by RT-PCR and ELISA. The expression of macrophage markers, wnt ligands and TGF β were analyzed in IFN γ -U937 treated cells, and IFN γ -U937 treated cells were co-cultured with HT29 cells. Results are expressed as fold induction (mean $\pm$ SEM, n $\geq$ 5). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test.

Results: The mRNA and protein expression of IFN γ was significantly higher in intestinal samples from B3 CD patients (19.3 $\pm$ 3.9 fold induction and 107 $\pm$ 36 pg/ml, respectively) than in controls (2.1 $\pm$ 0.3 fold induction and 12 $\pm$ 0.2 pg/ml, respectively) or B2 CD patients (9.8 $\pm$ 0.3 fold induction and 47 $\pm$ 1 pg/ml, respectively). IFN γ -U937 treated cells increased significantly the mRNA expression of *CD16* (1.9 $\pm$ 0.2), *CD86* (1.60 $\pm$ 0.1), *Wnt2b* (1.3 $\pm$ 0.1) and *TGF β* (2.2 $\pm$ 0.5) respect vehicle. HT29 cells co-cultured with IFN γ -U937 treated cells increase significantly the expression of *VIMENTIN*, *α SMA*, *SNAIL1* and *ZEB1* (3 $\pm$ 0.5, 24.2 $\pm$ 2.1, 2.7 $\pm$ 0.2, 2.1 $\pm$ 0.6, respectively) than in HT29 co-cultured with U937 vehicle (1.9 $\pm$ 0.3, 14.4 $\pm$ 2.1, 1.8 $\pm$ 0.2 and 0.6 $\pm$ 0.2, respectively).

Conclusion: IFN γ could be responsible the macrophage phenotype expressing CD86/CD16, and the macrophages may act as a source of EMT mediators in intestinal tissue from CD patients with a penetrating (B3) behavior.

Disclosure: Nothing to disclose

P0347

CHARACTERIZATION OF MUCOSAL CYTOKINE PROFILE IN ULCERATIVE COLITIS PATIENTS UNDER CONVENTIONAL AND ANTI-TNF-A TREATMENT

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Introduction: In Inflammatory Bowel Disease (IBD) intestinal homeostasis and inflammation are driven by cellular elements and innate-type soluble mediators that mediate both processes, with several cytokines exhibiting opposing roles, depending upon the specific setting and disease phase. A more focused analysis of the mucosal cytokine patterns could facilitate the design of selective targeted therapy and improve the decision on the specific treatment strategy with the end goal of promoting host health.

Aims & Methods: We aimed to characterize the expression patterns of inflammatory and regulatory cytokines in inflamed and adjacent uninflamed intestinal mucosal samples of Ulcerative Colitis (UC) patients. We also correlated their variation to inflamed Crohn's Disease (CD) samples, to biochemical, endoscopic and histological inflammatory activity, and to the undergoing therapeutical treatment.

11 UC patients were enrolled. Bioptic samples from inflamed (I) and not inflamed (NI) intestinal areas were obtained. I samples were also collected from 5 CD patients. Multiplex analysis for inflammatory and regulatory cytokines was performed. Serum CRP was assessed. Endoscopic Mayo score and histological Simplified Geboes Score (GS) were calculated.

Results: IL-1Ra, IL-6, IL-8, IL-17, IP-10, MCP-1, MIP-1a, MIP-1b resulted increased in UC I vs. UC NI areas. No significant differences were found for the remaining molecules. No mucosal cytokine changes were registered between conventional and anti-TNF-a regimens. IL-1b, IL-7 and IL-13 significantly differed between UC I and CD I samples. No difference with CRP levels was found. IL-7 resulted reduced in patients with endoscopic Mayo score $\geq$ 2. All the NI samples had a GS < 2A, while all the I specimens had a GS $\geq$ 2B. IL-1Ra resulted increased in the group with a GS $\geq$ 4.

Conclusion: Inflamed and adjacent not inflamed mucosal areas in UC patients share detailed inflammatory molecular pathways, but can be differentiated endoscopically and histologically on the base of specific cytokines levels. This underlines the complexity of the mucosal cytokine network in UC and highlights the major limitations of a single pro-inflammatory target therapeutic strategy in IBD.

Disclosure: Nothing to disclose

P0348

REGULATORS OF THE GUANYLATE CYCLASE PATHWAY ARE POTENTIAL NOVEL MARKERS OF MUCOSAL HEALING IN IBD

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Introduction: Intestinal Guanylate cyclase C (GC-C) expressed in intestinal epithelial cells has been shown to have a role in gut homeostasis. The downstream effects of activation of GC-C are due to production of cyclic-GMP. GC-C is encoded by the gene *GUCY2C*, mutations in which are implicated in Familial Diarrhoea Syndrome and reported as risk factors for Crohn's disease. *GUCY2C* and its activator, *GUCA2A* have been shown to be downregulated in IBD. We hypothesised that regulation of this pathway might be important in endoscopic remission & response, to therapy.

Aims & Methods: The aim of the study was to understand the changes in transcription factors in GC-C pathway in relation to disease activity, and response to therapy in IBD.

44 (UC=28, CD=16) patients with IBD & 7 patients as controls at the University Hospitals Birmingham, UK were recruited under informed consent. All patients had disease activity recorded at colonoscopic examination and intestinal biopsies collected for analysis. Mucosal healing was defined as Mayo Endoscopic Subscore=0 (UC) and SES-CD < 6 (CD). 14/44 patients (UC=7, CD=7) had matched baseline and 12-week post-biologic therapy assessment [anti-TNFa=11, anti-integrin=3]. Intestinal biopsies were analysed by 3'RNA-sequencing using the Illumina Nextseq sequencer. FASTQ files were generated through BaseSpace and reads de-multiplexed, trimmed, aligned, and quantified using the GeneGlobe (Qiagen) workflow. Expression was compared between groups using either Wilcoxon test, ANOVA or Kruskal-Wallis with Dunn post-hoc analysis as appropriate.

Results: Expression of Guanylate cyclase activators *GUCA2A* and *GUCA2B* in patients who showed mucosal healing (n=18) was equivalent to controls, but *GUCA2A* was down-regulated in those with active disease (n=12) (non-healing) (P=0.006). The same pattern was observed for transcriptional regulators of *GUCY2C*, including *HNF4A* (P=0.025) and *CDX2* (P=0.006) (Fig 1A). Correspondingly, *GUCY2C* was reduced in non-healing mucosa, although the difference was not significant.

In patients who had colonoscopic response to biologic therapy, both *GUCA2A* (P=0.023) (Fig 1B) and *GUCA2B* (P=0.012) were increased at follow-up but no change was observed for those who did not respond.

Figure 1- Results of *GUCA2A*, *HNF4A* and *CDX2* expression in mucosal healing & response to therapy (Image not allowed during abstract submission).

Conclusion: Our findings suggest that expression of the Guanylate Cyclase pathway may be involved in mucosal healing and may indicate mucosal response after biologics.

Disclosure: Nothing to disclose

P0349

VALIDATION OF GROWTH STUDY IN A PROSPECTIVE INCEPTION COHORT OF PEDIATRIC CD PATIENTS

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Introduction: Most patients with Crohn's Disease (CD) develop stenosing or fistulizing disease during their disease course. GROWTH cohort evaluated predictors to SFR and predictors to later relapse in patients those achieved SFR in 4 month and found association between CRP at baseline to SFR at 4 months and association between SFR with normal ESR/CRP at 4 months to SFR at 12 months. They found correlated between calprotectin, CRP and PCDAI levels at 4 month to later relapse. We aimed to validate the GROWTH model to predict long-term disease outcomes in a prospective inception cohort of children with CD.

Aims & Methods: Children (0-18 years) with new diagnosis of CD were prospectively followed from baseline to 4 and 12 months thereafter as well as at end of follow-up. Management was standardized based on ESPGHAN-ECCO treatment guidelines of PIBD. The primary outcome was steroid-free clinical remission (SFR) defined as weighted pediatric Crohn's disease activity index (wPCDAI) < 12.5 points. Other outcomes to predict were evidence of stricturing or fistulizing disease as well as time to biologic treatment. Bowel imaging and/or colonoscopy, were performed as clinically indicated.

Results: A total of 82 children were included (mean age 13±4.7 years; 38 (46%) with mild disease and 44 (54%) with moderate-severe disease, median follow-up 13.2 month (10.8-23.8)). Repeated MRE, CTE, bowel US, or colonoscopy were performed in 64 (78%) of patients within one year and 73 (89%) of patients at end of follow-up.

SFR was achieved in 36 (44%) patients at 4 months and 51 (64%) at 12 months. SFR with normal ESR/CRP was achieved in 25 (30%) and 39 (49%) at 4 and 12 month, respectively. SFR at 12 months was higher in those with SFR at 4 months (29 (81%)) compared with those without 20 (43%; p=0.001).

The prevalence of stenosis and internal fistulizing disease was 16 (20%) and 3 (4%) one year after diagnosis and 22 (28%) and 6 (8%) at the end of the follow up, respectively. The treatment of 44 (53%) children escalated to biologic treatment, 17 (21%) of whom within three month from diagnosis (median time to biologics: 4.5 months (1.5-9.9)).

Unlike found in the GROWTH cohort, we could not replicate the finding of the GROWTH study of an association between baseline CRP levels and SFR at 4 month (4.1 mg/L (IQR 1.5-6.2) in responders vs 2.2 mg/L in non-responders (0.6-4.8), p=0.17). Similarly, SFR with normal CRP at 4 months did not predict SFR at 12 month, although this was in the trend range (OR=2.6 (95%CI 0.9-7.5), p=0.07).

Similar to GROWTH, we did find an association between calprotectin level and relapse (394 mcg/g (IQR 135-1093) vs 1225 mcg/g (293-2578); p=0.04), but we could not find an association between CRP>20 and relapse (none patients with SFR at 4 month and CRP>20).

In our cohort we found that SFR one year after diagnosis was associated with higher median wPCDAI at 4-month (5 (IQR 0-25) in responders vs 15 in non-responders (7.5-25), p=0.002) and but not with wPCDAI level at baseline.

The need for biologics was associated in a Cox regression model with family history of IBD (HR 4.7 (95%CI 1.5-15.3), $p=0.01$), extraintestinal manifestations (HR 5.0 (1.6-15.4), $p=0.01$) and moderate-severe disease at baseline by wPCDAI (HR 1.9 (1.1-3.7), $p=0.05$).

Conclusion: SFR is achievable in most patients at 1 year but 27% develop bowel damage. Several variables may predict treatment response and complications, but we did success to validates only partially of the GROWTH cohort model. We found association between wPCDAI and calprotectin levels at 4 months to relapse, but note between CRP and relapse or SFR at 12 months.

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P0350

AZATHIOPRINE AND ANTI-TNF THERAPIES AFFECT THE GUT MICROBIOME DIFFERENTLY IN IBD PATIENTS

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Introduction: Therapeutic responses in inflammatory bowel disease (IBD) seems to be affected by the microbial ecosystem.

Aims & Methods: Longitudinal microbiome changes in IBD patients undergoing therapy with either azathioprine (AZA) or anti-tumor-necrosis-factor (anti-TNF) antibodies were assessed.

We predicted the metabolic microbial community exchange and linked it to clinical outcome. Blood and fecal samples were collected from 65 IBD patients at 3 timepoints: baseline and after 12 and 30 weeks on therapy. Clinical remission was defined as i.e. CDAI < 150 in Crohn's disease (CD), partial Mayo score < 2 in ulcerative colitis (UC) and fecal calprotectin values < 150 µg/g and C-reactive protein < 5 mg/dl.

We performed 16S rRNA amplicon sequencing. To predict microbial community metabolic processes, we constructed multi-species genome-scale metabolic network models.

Results: Longitudinal changes in taxa composition at phylum level showed a significant decrease of Proteobacteria and an increase of Bacteroidetes in CD patients responding to both therapies. At family level, Lactobacilli were associated with persistent disease and Bacteroides abundance with remission in CD. Paired Bray-Curtis distance between baseline and follow-up timepoints was significantly different for UC patients treated with anti-TNF antibodies.

The *in-silico* simulations predicted that butyrate production capacity of patients in remission is 1.7-fold higher compared to patients without remission ($p=0.041$). In this model, the difference of butyrate production between patients in remission and patients without remission was most pronounced in the CD group treated with AZA ($p=0.008$).

Conclusion: The microbial ecosystem plays an important role of therapeutic efficacy in IBD and is most pronounced in CD patients undergoing AZA treatment. In-silico simulation identifies microbial butyrate synthesis predictive of therapeutic efficacy in IBD.

Disclosure: Nothing to disclose

P0351

SEROLOGICAL MARKERS OF EXTRACELLULAR MATRIX REMODELING REFLECTS ENDOSCOPIC DISEASE ACTIVITY AND SEVERITY IN CROHN'S DISEASE AND ULCERATIVE COLITIS

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Introduction: Extracellular matrix remodeling is a key process of tissue homeostasis in which old, damaged, and dysfunctional proteins are being degraded and replaced with newly synthesized ECM. Disease activity in IBD can lead to dysregulated balance between formation and degradation which results in structurally and qualitatively different intestinal ECM and altered bowel function. High levels of protein degradation and formation fragments are being released into the bloodstream.

Aims & Methods: The aim of the study was to investigate serological biomarkers of type III, IV and V collagen degradation and formation, and their association with disease activity, severity, and extension in IBD.

In this cross-sectional study, we have measured ECM remodeling biomarkers in 162 IBD patients (110 CD and 52 UC) and 29 healthy donors (HD). Biomarkers of type III collagen degradation (C3M) and formation (PRO-C3), type IV collagen degradation (C4M) and formation (PRO-C4), type V collagen formation (PRO-C5) were measured in serum by ELISA. Inflammatory activity was assessed using endoscopic scores SES-CD, and modified Mayo endoscopic score (mMES). The mMES score was used to add information about disease extension to the severity of inflammation. Clinical and biochemical disease activity was defined using Harvey Bradshaw Index (HBI), partial Mayo score (pMayo) and CRP.

Results: The average age of CD and UC patients was 36 (27.75-46) and 37 (24-49). CD and UC patients were similar in BMI, use of immunosuppressive and biological therapy. There were more male patients (60% vs. 53.84%) and more smokers (21.81% vs. 13.46%) in CD than in UC group. Both CD and UC had a similar proportion of patients with moderate to severe disease (30% vs. 30.33%). In CD C4M, PRO-C4 and PRO-C5 were elevated in moderate to severe or mild disease on endoscopy, and in UC C3M was additionally elevated ($p < 0.05$). PRO-C3 levels were lower with higher disease activity in CD and UC ($p < 0.05$). Highest diagnostic value of single biomarkers was in discriminating endoscopically moderate to severely active disease in CD (PRO-C3, C3M/PRO-C3 and C4M with an AUC of 0.70(0.53-0.83), 0.73 (0.56-0.85) and 0.69 0.54-0.81, respectively) and UC (C3M, C3M/PRO-C3 and C4M with an AUC 0.86 0.54-0.98, 0.80 0.48-0.97 and 0.76 0.48-0.96, respectively).

In combination, C4M and C3M/PRO-C3 had a diagnostic value with an AUC 0.93 (0.66-0.90) in CD and an AUC of 0.94 (0.65-0.99) in UC. Combination of C4M and C3M/PRO-C3 correlated with mMES ($r=0.82$) and with SES-CD ($r=0.56$).

Conclusion: In conclusion, this study confirms for the first time that ECM remodeling quantified by serological markers of collagen degradation and formation reflects endoscopically active disease in UC and CD, especially collagen type III turnover (C3M/PRO-C3) and increased basement membrane remodeling quantified by type IV collagen degradation and formation, but also formation of type V collagen. A combination of the biomarkers C4M, C3M, and PRO-C3 could be used in differentiating moderate to severe endoscopic disease from patients in remission. Also, this combination could be used to assess the disease severity, especially in UC, where CRP is of less significance. Further prospective studies on a larger sample of patients with endoscopic disease activity indices are needed to confirm the current findings.

Disclosure: Nothing to disclose

P0352

EVALUATION OF THE ROLE OF ENTERIC NEURONS AND INTERSTITIAL CELLS IN COLONIC INFLAMMATION IN THE MOUSE MODEL OF DSS-INDUCED COLITIS

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Introduction: Ulcerative colitis (UC), which belongs to inflammatory bowel diseases (IBD) is a chronic condition that significantly affects patients' quality of life. Not fully understood etiology and limited efficiency of treatment force further studies on IBD. The interstitial cells like neurons, interstitial cells of Cajal (ICC) and telocytes may play an important role in IBD pathogenesis, being involved in tissue repair, immune regulation, local intercellular signaling and intestinal motility regulation. These promising properties of interstitial cells suggest their potential as future target in IBD treatment, however currently available research evaluating the changes in interstitial cells populations, particularly in the mouse models of IBD is scarce.

Aims & Methods: The aim of this study was to assess the differences in enteric neurons and selected interstitial cells (ICC and telocytes) populations in non-inflamed (controls) and inflamed (dextran sulfate sodium (DSS)-induced colitis) mouse colon mucosa. Furthermore, a comparison was made with inflamed mouse colon mucosa in DSS-treated mice receiving mesalazine (5-aminosalicylic acid, 5ASA).

In our study we divided 30 male Balb/C mice into control and two DSS-treated groups: DSS+0.9% NaCl ('DSS-only') and DSS+5ASA (10 mice each). The DSS groups underwent a 7-day treatment with orally administered 3% DSS water drinking solution from day 0 to day 4, which was then exchanged for water. The 5ASA treatment was administered between days 3 and 6 by intragastric administration. On day 7, mice were sacrificed and colon samples were taken for macroscopic evaluation of the inflammation score and immunohistochemical examination. The enteric neurons were identified as PGP 9.5 positive cells, ICC were c-kit positive and telocytes were CD34 and PDGFRα double-positive cells.

Results: Both DSS groups had significantly higher macroscopic inflammation score than control. The 5ASA group had notably lower score than DSS-only, however without statistical significance. The examined enteric neurons' populations were located mainly in muscular and external part of the wall, with differences in distribution and morphology between the groups. Quantitatively, neurons were more abundant in DSS-only group than in control. The 5ASA treatment caused neurons decrease comparing to DSS-only group. There were no significant differences in ICC populations among all three groups, however clear decreasing tendency in DSS-

only group was observed. Moreover, we observed changes in ICC morphology and local distribution. The telocytes populations within the colon were similar in control and DSS-only group with significant higher abundance in the intestinal crypts than subepithelial sheath. Interestingly, the 5ASA group had significantly fewer telocytes in both locations.

Conclusion: The impact of enteric neurons and interstitial cells populations on inflammation in the mouse colon was clearly observed. Most noteworthy, the distribution of telocytes suggests their role in adaptive reaction of the mucosa and also possible involvement in regeneration and healing. Moreover, the significant increase in neurons population in DSS-only group comparing to control suggests neuronal character of inflammation in the course of UC. In agreement with this hypothesis, we speculate that significantly lower neurons' population after 5-ASA treatment comparing to DSS-only group may correlate with lower inflammation score in 5-ASA-treated colons.

To the best of our knowledge, this is the first study on the possible role of interstitial cells in the pathogenesis of IBD in mouse.

Disclosure: Nothing to disclose

P0353

OVERABUNDANCE OF SERUM IMMUNOGLOBULIN G SPECIFIC TO *ESCHERICHIA COLI* STRAINS AS ONE OF THE FEATURES OF CROHN'S DISEASE

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Introduction:

Crohn's disease (CD) is characterized by increase of the relative abundance of Proteobacteria, in particular *Escherichia coli*. An impaired immune response against intestinal bacteria leads to chronic gut inflammation [1]. Although CD is associated with a Th1 T cell-mediated response, there is also a humoral immune response [2]. Immunoglobulin G (IgG) is the most common type of antibody to control infection in human organism. Patients with active disease and shortly after remission have an increased percentage of IgG-coated faecal anaerobic bacteria compared with non-inflammatory controls [3].

Aims & Methods: The aim of the study was to assess the level of circulating IgG in bloodstream of CD patients and healthy donors (control) and the IgG-binding capacities to different *E. coli* strains isolated from their feces. *E. coli* strains (n=17) and serum samples from CD patients (n=7) and healthy donors (n=3) were taken from the collection created and characterized earlier [4]. Serum IgG specific for *E. coli* antigens were analyzed by ELISA in patients with Crohn's disease and non-inflammatory controls. Differences in the IgG levels were evaluated using the nonparametric Kruskal-Wallis test. P value > 0.05 was accepted as statistically significant level.

Results: In this study the serum level of total IgG was not significantly different between CD patients and non-inflammatory controls, but *E. coli* strains isolated from the same individuals shown different reactivity to the

serum samples. Only 4 of 17 strains tested (3 from CD patients and 1 from healthy donor) were significantly more reactive to IgG of patients sera than those of controls. Although these high-IgG-binding strains are more immunogenic they possess the same virulent potential as the other ones [4]. It is possible that they have specific surface antigens recognized by immune system in CD patients but not in controls. The lack of difference in IgG binding level among the other strains may be accounted for tolerance of the immune system for endogenous fecal bacteria without certain epitopes. It is interesting that one CD patient showed high IgG reactivity with all *E. coli* strains, regardless of their origin. Perhaps, in this individual antibody response was caused by common *E. coli* antigen which could lead to more severe manifestations of the disease.

Conclusion: The testing of *E. coli* strains reveal that some bacteria are more prone to bind to CD serum IgG than those from healthy donors. It can be assumed that the development of the disease, in addition to imbalance in bacterial community, is associated with altered interaction between the intestinal bacteria and human immune system. So further studies on identification of IgG-binding proteins may shed light on CD pathogenesis and reveal new candidates for therapeutic targets.

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P0354

TRANSCRIPTOMIC INSIGHT INTO IN VITRO INTERACTION OF *ESCHERICHIA COLI* WITH IMMUNOGLOBULIN A AS A MODEL OF THE INFLAMMATORY BOWEL DISEASE PATHOGENESIS

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Introduction: Immunoglobulin A (IgA) is secreted by the intestinal mucosa to prevent invasion of pathogenic and commensal bacteria and inflammation of the epithelium. Fecal samples of patients with inflammatory bowel diseases (IBD) contain a greater proportion of bacteria coated with IgA compared with healthy ones [1]. IgA-coated microbes increase susceptibility to intestine inflammation after transferring into mice [2]. IBD is often accompanied by intestinal dysbiosis, in particular an increased abundance of *Escherichia coli* [3]. The previous study revealed that the pathogenicity and virulence potential of *E. coli* strains isolated from feces of IBD patients does not differ from strains of healthy subjects [4].

Aims & Methods: The aim of the study was to characterize the shifts of *E. coli* Nissle 1917 transcriptome profile in response to interaction with secretory IgA.

The incubation of *E. coli* Nissle 1917 with and without (control) monoclonal IgA (55 mcg/ml) for 1 hour at 25°C in phosphate buffered saline (PBS) was performed. The experiment was carried out in two biological replications. Total RNA was extracted after cell washing in PBS and libraries were prepared for sequencing on NextSeq 500 platform (Illumina, USA). Resulting reads were aligned with Bowtie2, assigned to genes and counted with featureCounts. Differential expression analysis was performed with DeSeq2 package.

Results: Incubation of *E. coli* with secretory IgA led to a statistically significant change in the expression of 68 genes (*p* adjusted < 0.05). Only two genes were downregulated in the experiment with antibodies compared to control. These genes encode carbamate kinase (log2FoldChange (log2FC) = -1.10) and alternative ribosome-rescue factor A (log2FC = -1.22) of *E. coli*. The expression of the remaining 66 genes was significantly increased in the experimental group. A number of genes for the bacterial stress adaptation increased their expression in IgA condition compared to control. RNA polymerase sigma factor RpoS was upregulated (log2FC = 0.98). This factor is the main regulator of transcription of genes involved in the stress response. An increase in the expression of genes for nucleic acid repair, fatty acid beta oxidation, glycolysis, citric acid cycle, and transport of metabolites, carbohydrates, and fatty acids has been found. Porin genes *ompA*, *ompC*, *ompD* (log2FC = 1.09, 1.04, 0.84, respectively) were upregulated in bacteria after incubation with IgA. Porins are known to play a role in adhesion of bacteria to the epithelium. For *E. coli* incubated with antibodies, an increase in the expression of fimbriae genes *fimA* (log2FC = 0.93), *fimC* (log2FC = 0.99) was observed. Using these fimbriae, bacteria are able to colonize human intestinal epithelium and form biofilms. The intestinal mucosa in IBD patients produces more IgA than in controls, which can stimulate commensal *E. coli* to synthesize more adhesion structures. This shift can lead to an enhancement in the ability of *E. coli* to adhere to intestinal epithelium, which can provoke inflammation.

Conclusion: Interaction of *E. coli* with large amounts of IgA produced by intestinal mucosa of IBD patients may lead to increase of bacterial adhesion, causing epithelial inflammation. Porins and fimbriae of *E. coli* may become a potential therapeutic target for IBD treatment after verification in further research.

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P0355

KNOCKDOWN OF MUC1 AND MUC13 IN INFLAMED INTESTINAL EPITHELIAL CELLS AFFECTS EXPRESSION OF KEY GENES INVOLVED IN INTESTINAL BARRIER HOMEOSTASIS

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Introduction: The intestinal mucosal barrier consists of a thick mucus layer, a single layer of epithelial cells and the lamina propria interacting with immune cells. Secreted and transmembrane mucins are major components of the mucus barrier. Besides providing protection to the underlying epithelium, transmembrane mucins participate in the intracellular signal transduction¹. Of particular interest are MUC1 and MUC13, which are increasingly expressed in the colon during the course of colitis in mice and in the inflamed colonic mucosa of patients with inflammatory bowel diseases². Aberrant expression of mucins could disrupt barrier integrity resulting in chronic inflammation and progression to cancer³. Nevertheless, the signaling pathways related to aberrant MUC1 and MUC13 expression remain poorly understood. This study aimed to explore and identify potential upstream regulators and downstream effectors of epithelial MUC1 and MUC13 expression during inflammation focusing on intestinal barrier-related genes.
Aims & Methods: LS513 cells were transfected with siRNA targeting MUC1 and MUC13, after which they were stimulated with 20 ng/mL TNF-α or IL-22 for 24h. Untreated cells and cells transfected with negative control siRNA were included as controls. siRNA transfection and cytokine stimulation were validated by qPCR. Subsequently, Illumina mRNA sequencing was performed to investigate differentially expressed genes (DEGs) and the corresponding canonical pathways involved (4 samples/condition). After data processing (using Trimmomatic, STAR and DESeq2 tools), pathway analysis was performed using Ingenuity Pathway Analysis software. Additionally, DEGs were further explored individually for a potential role in directly modulating intestinal barrier integrity.
Results: Transcriptome analysis of untreated cells silenced for MUC1 or MUC13 (vs unsilenced controls) revealed respectively 2006 and 3232 candidate downstream effectors. When silenced for MUC1 or MUC13, stimulation with TNF-α resulted in 39 and 103 DEGs and with IL-22 in 857 and 88 DEGs respectively (Table 1). This was associated with the enrichment of molecular pathways involved in inflammation (e.g. IL-1, IL-6, IL-7, IL-15, IL-17 signaling), cell invasiveness (e.g. cancer signaling, regulation of the epithelial-mesenchymal transition pathway) and cell-cell interactions (e.g. cell-cell junction signaling, tight junction signaling). Moreover, a targeted search on intestinal barrier-related genes showed the differential expression of several claudins, cadherins and tubulins (Table 1). Finally, the NFκB complex and STAT1 were identified as potential upstream regulators of MUC1 and MUC13 expression during TNF-α and IL-22 stimulation.
Conclusion: Silencing of MUC1 and MUC13 in intestinal epithelial cells resulted in cytokine-dependent and -independent changes in gene expression, including genes involved in the modulation of intestinal barrier integrity. These results highlight their importance in co-regulating intestinal barrier function.

Mucin	MUC1		MUC13	
Cytokine	TNF-α		IL-22	
Fold change upon cytokine stimulation (p<0.05)	1.8		11.2	
% mucin knockdown upon siRNA transfection	76		70	
Number of DEGs compared to control siRNA	39		857	
Intestinal barrier related genes (Fold change > [1.5]; p < 0.05; q < 0.1)	CLDN7		CLDN2 CLDN3 CLDN4 TUBA1C TUBA4A TUBB	
			CLDN1 CLDN2 CLDN7 TUB1A1 TUBB3 PATJ	
			CLDN3 CLDN4 CDH3 PCDH1 TUBB3	

[Table 1: Effect of mucin knockdown and cytokine stimulation on gene expression in LS513 cells]

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Disclosure: Nothing to disclose

P0356

NO ASSOCIATION BETWEEN POST-INFLAMMATORY PSEUDOPOLYPS AND COLORECTAL NEOPLASIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Patients with longstanding inflammatory bowel disease (IBD) are at increased risk of development of colorectal dysplasia and cancer. Guidelines recommend surveillance colonoscopies at regular intervals. Post-inflammatory “pseudo”polyps (PIPs) are an endoscopic hallmark of previous severe inflammation. Current European guidelines advocate that their presence is used to risk stratify patients. Current published data is conflicting as to their association with advanced colorectal neoplasia (ACRN, high grade dysplasia or colorectal cancer).
Aims & Methods: Our primary objective was to assess the occurrence of ACRN according to PIP status. Retrospective study of IBD patients who underwent colonoscopic surveillance, from January 1st, 2009 to December 31st, 2018, from an academic teaching hospital. Eligible IBD patients had confirmed colonic disease with duration of ≥8 years or any duration if diagnosis of primary sclerosing cholangitis and no history of ACRN or colectomy. Clinical data, endoscopy and histology reports were obtained from patient’s electronic health record.
Results: Of the 237 eligible patients, 44 had PIPs (18.5%). No significant association was found between the presence of PIPs and ACRN OR 2.3 [95% CI 0.2 - 36.7], p=0.57, with ACRN occurring 1.4% and 0.6% of patients with and without PIPs respectively. There was a significant association be-

tween patient with PIPs and colectomy, OR 7.3 [95% CI 1.4 - 36.9], $p=0.017$. Colectomy occurred in 9.1% ($n=4$) of patients with PIPs compared with 2% of those without ($n=4$).

Conclusion: This study further adds to growing evidence that endoscopic finding of PIPs are not associated with ACRN. This observation should be taken into account in development of future guidelines.

Disclosure: Nothing to disclose

P0357

NAD IMMUNOMETABOLISM IN NK CELL BIOLOGY DURING INTESTINAL INFLAMMATION

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Introduction: Immunometabolic pathways such as the NAD⁺ salvage pathway are important regulators of immune cell function. For instance, blocking this pathway in macrophages results in a more anti-inflammatory M2 phenotype. Natural killer (NK) cells represent a subset of innate lymphoid cells (ILCs), capable of direct cytotoxicity, independent of antibody mediation but also shaping immune responses and orchestrating other subsets of immune cells. Nevertheless, only little is known about their role in inflammatory bowel diseases (IBD). In this study we investigated (i) the expression and activation state of the NAD⁺ salvage pathway during NK cell activation, (ii) the effect of FK866, a small molecule inhibitor of the key enzyme of the NAD⁺ salvage pathway (nicotinamide phosphoribosyl-transferase; NAMPT, PBEF/Visfatin) on NK cell function and (iii) the characteristics of the human mucosal NK cell repertoire of the colon in the steady state as well as during intestinal inflammation.

Aims & Methods: Human peripheral blood CD56⁺ cells were obtained using magnetic cell sorting (MACS). These cells were then treated with interleukin-2 +/- FK866. Expression of IFN-gamma and NAMPT was assayed using quantitative PCR and intracellular flow cytometry. Subcellular localization of NAMPT during NK cell activation was tracked using confocal laser scanning microscopy. A CD107a degranulation assay was performed to quantify NK cell killing activity. Human colonoscopy biopsies were obtained from IBD patients and non-IBD controls and subjected to flow cytometry, immunohistochemistry and immunofluorescent laser scanning microscopy.

Results: Activation of peripheral blood CD56⁺ cells with interleukin-2 strongly induced the key enzyme of the NAD⁺ salvage pathway, NAMPT. This was accompanied by a drastic increase of IFN-gamma secretion in vitro. Treatment with the NAMPT inhibitor FK866 resulted in a drastic suppression of this activation state. Interestingly, NAMPT expression was increased after FK866 treatment, but activity of NAD-dependent enzymes was diminished. This was accompanied by translocation of NAMPT from the cytoplasm into the nucleus. In the CD107a degranulation assay, NAMPT inhibition effectively interfered with NK cell killing activity. Additionally, using colonoscopy biopsies from patients with ulcerative colitis and healthy controls we a thorough flow cytometric descriptive analysis of the mucosal NK cell repertoire in the steady state and during intestinal inflammation was generated.

Conclusion: Immunometabolic pathways such as the NAD⁺ salvage pathway are central to NK cell activation and function and represent an attractive putative therapeutic target in IBD.

Disclosure: Nothing to disclose

P0358

CLOSTRIDIUM DIFFICILE INFECTION IN IBD PATIENTS HOSPITALIZED IN A TERTIARY CENTER

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Introduction: Clostridium difficile infection represents a major concern in the inflammatory bowel disease (IBD) patients, due to its increasing reported rates and the consequences on the following evolution of the underlying disease. The immunosuppressive medication, reduction in gut microbial diversity with an increase of pro-inflammatory species are the main causative factors.

Aims & Methods: Our goal was to assess the Clostridium Difficile (C Diff.) infection rate among IBD patients registered in a tertiary Gastroenterology Department, as well as to determine the potential risk factors involved and the impact on IBD course. We have retrospectively analysed medical records of the IBD patients admitted in our tertiary center between January 2017 and December 2019, registering epidemiological and phenotypical characteristics, IBD treatment during the previous year and following the C Diff episode, subsequent IBD management and complications.

Results: Out of 1025 IBD patients hospitalized, 55 (5.41%) had a C. Diff. enterocolitis, 38 patients with ulcerative colitis (UC) and 17 with Crohn disease (CD). 40% were male and the mean age was 46 years. Most UC patients had extensive E3 disease (65.78%). 70.58% in the CD group had colonic disease and 35.29% ileo-colonic extension. According to disease severity Mayo and CDAI scores, prior to the C Diff diagnosis, 63.15% of the UC patients had moderate disease and 18.42% severe disease. On the other hand, among the CD patients, 47.05% of them suffered from severe disease and 41.17% moderate disease. Severity of the disease at the time of C. Diff. enterocolitis was predictive for a subsequent severe IBD flare thereafter ($p=0.008$). 25.43% patients were treated with a biological agent and 32.72% had followed a glucocorticoid course in the past year of the C Diff infection. Corticosteroid use in the previous year was strongly correlated to the infection relapse ($p=0.02$) and the need of a subsequent IBD treatment escalation ($p=0.01$). None of the other treatment regimens within the past year of the infection were associated with poor outcome after the acute episode. The association of Vancomycin and Metronidazole was the elective treatment (52.72%) of the C. Diff. infection. Vancomycin monotherapy of C. Diff. episode was associated with the subsequent necessity of IBD treatment escalation ($p=0.03$). Following the Clostridium infection, colectomy was performed in 10.90% of the patients. Mortality rate in our study group of C. Diff. infection complicating the course of IBD was 3.63% (2 patients).

Conclusion: The use of corticoid treatment in the previous year, the severity of the underlying disease and the Vancomycin monotherapy are associated with a poor outcome in IBD patients who suffered a Clostridium difficile infection.

Disclosure: Nothing to disclose

P0359

NOVEL INSIGHT INTO MECHANISM OF HEALING OF EXPERIMENTAL COLITIS BY INTESTINAL ALKALINE PHOSPHATASE IN OBESE MICE SUBJECTED TO FORCED TREADMILL EXERCISE. INVOLVEMENT OF OXIDATIVE STRESS, PROINFLAMMATORY BIOMARKERS AND INTESTINAL BARRIER PROTEINS

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Introduction: The role of adiposity in inflammatory bowel disease (IBD), which presents mainly as Crohn's disease (CD) and ulcerative colitis (UC) remains largely unknown. Both diseases characterized by a cyclical nature alternating between active and quiescent states, that markedly diminish physical functioning and quality of life in patients. Exercise of different intensity was recommended as the alternative therapy in prevention and healing of these disorders. An important apical brush border enzyme, the intestinal alkaline phosphatase (IAP) released from cells walls during stressful events maintains tight junction and barrier integrity but whether IAP treatment can influence the course of experimental colitis in obese mice with forced treadmill exercise has been little elucidated.

Aims & Methods: Two major series of C57BL/6 male mice were fed *ad libitum* high fat diet (HFD, 70% energy from fat, series A) or standard diet (SD, 10% energy from fat, series B) (Altromin, Lage, Germany) for 12 weeks and subjected to forced treadmill exercise (15 min/day, 6 wks., Panlab, Harvard Apparatus, MA, USA) with or without the intragastric treatment with AP (200 U/day) and trinitrobenzene sulfonic acid (TNBS) colitis was induced. Following colitis, the colonic blood flow (CBF) was examined by Laser Doppler flowmetry, the disease activity index (DAI), histology of intestinal mucosa, the caloric intake and muscle strength (BIO-GS3 device, Canada), the oxidative stress markers MDA+4-HNE, GSH+GSSG contents and SOD activity were evaluated in colonic mucosa. The colonic expression of proinflammatory biomarkers IL-1 β , TNF- α , MCP-1 and IL-12 mRNAs, the protein expression of phospho-NF κ B, metalloproteinase (MMP)-9, iNOS, inhibitor of MMPs TIMP-1, the tight junctions protein occludin, ZO-1, and adipomyokine irisin were evaluated by qPCR and Western blot, respectively. Proinflammatory markers in plasma: IL-2, IL-6, IL-10, IL-12p70, IL-17, TNF- α , MCP-1 and leptin was performed using Luminex microbeads fluorescent assays.

Results: In sedentary SD mice the DAI was accompanied by a significant fall in CBF and muscle strength and these changes were exacerbated in obese mice. Treadmill exercise exacerbated the DAI activity in obese mice and decreased CBF, vs. SD fed mice ($P < 0.05$) and significantly increased the MDA+4-HNE, GSH+GSSG contents, SOD activity, the mRNAs expression of IL-1 β , TNF- α , MCP-1, IL-12 mRNAs and protein for phospho-NF κ B, MMP-9 and iNOS ($p < 0.05$). In obese mice, the downregulation of occludin, ZO-1 and TIMP-1 protein expression was observed. Treatment with IAP decreased DAI, improved relative muscle strength and significantly reduced the mRNA expression of IL-1 β , TNF- α , MCP-1, IL-12 and downregulated phospho-NF κ B, MMP-9 protein while increasing protein expression of occludin and ZO-1 and these effects were significantly more pronounced in mice fed HFD vs. SD.

Conclusion: Forced treadmill exercise exaggerates the severity of colonic damage in obese mice *via* mechanism involving the fall in colonic microcirculation due to oxidative stress in colonic mucosa and the upregulation of local and systemic proinflammatory biomarkers. Treatment with

IAP ameliorates the worsening effect of forced exercise on the course of experimental colitis due to the attenuation of oxidative stress and down-regulation of proinflammatory biomarkers and the preservation of intestinal barrier protein in colonic mucosa. The efficacy of IAP might be novel alternative in the treatment of clinical IBD.

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P0360

INCREASED RISK OF INFLAMMATORY BOWEL DISEASE IN INDIVIDUALS WITH HIV IN BOTH DANISH AND US COHORTS

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Introduction: The pathophysiology of HIV and Inflammatory Bowel Disease (IBD) are distinct, but closely interwoven. Despite this, few epidemiological studies have examined the risk of IBD development in HIV. Using two national datasets we aimed to assess and quantify the risk of IBD in HIV.

Aims & Methods: Using the Danish national register we matched 7,949 people living with HIV (PLWH) with 397,450 HIV-negative controls based on age and sex, and followed these individuals for 6,475,366 person-years. Competing risk Cox regression analyses were used to estimate hazard ratios (HR) for the development of IBD in PLWH versus HIV-negative individuals after adjusting for year of diagnosis. Using Explorys, a large claims dataset; we aimed to confirm this observation by comparing the prevalence of de-novo IBD over a 10-year period (2009-2019) in PLWH (238,870) versus HIV-negative (72,714,360) individuals in the US. Explorys results are reported as odds ratios (OR) with 95% Confidence Intervals (CI).

Results: The cumulative incidence of IBD among PLWH in Denmark was low (1.02%), and comparable to the prevalence of de-novo IBD among PLWH in the US (0.67%). The mean time from HIV diagnosis to IBD diagnosis was 6.8 years (range 0.06 to 21.9 years). The risk of developing IBD was significantly increased among PLWH in Denmark (HR 2.00, 95% CI 1.54-2.61) and the US (OR 1.41, 95% CI 1.35-1.49). Among PLWH, the majority of IBD cases were ulcerative colitis (70%) in Denmark with a slight predominance of Crohn's disease (54%) in the US. In the Danish register, the risk of IBD among PLWH was numerically higher in the pre-antiretroviral therapy (ART) era (1977-1996; HR 2.15, 95% CI 1.39-3.31) versus post-ART era (1997-2018; HR 1.87, 95% CI 1.33-2.61). An increased risk was observed among males with HIV in Denmark (Female: HR 0.72, 95% CI 0.32-1.61; Male: HR 2.47, 95% CI 1.86-3.28) whereas in the US this was observed among females with HIV (Female: OR 1.87, 95% CI 1.76-1.99; Male: OR 1.09, 95% CI 1.02-1.18).

Conclusion: Using two national datasets with differing population characteristics and HIV prevalence, we observed an increased risk of IBD among PLWH. This risk appeared reduced after the availability of ART. Further research into the interplay between HIV and IBD, and the impact of ART on this is required.

Disclosure: Nothing to disclose

P0361

COMPLICATIONS AND ADVERSE EFFECTS RELATED TO SURGICAL AND MEDICAL TREATMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A PROSPECTIVELY RECRUITED POPULATION-BASED COHORT

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Introduction: Medical adverse effects and surgical complications have been reported during treatment of patients with inflammatory bowel diseases. There is however a shortage of studies describing these in the same cohort of patients.

Aims & Methods: To describe medical adverse effects and surgical complications in a prospectively followed population based cohort of patients followed for at least 10 years. All newly diagnosed patients with ulcerative colitis and Crohn's disease in the county of Uppsala between 2005 and 2009 were prospectively followed. At the end of 2019, the medical notes were scrutinized and all medical adverse effects and postoperative surgical complications were registered. To qualify as an adverse effect, the drug should have been withdrawn, not only dose adjusted.

Results: 330 patients with ulcerative colitis (UC) and 154 patients with Crohn's disease (CD) in all age groups were included in the cohort. Four hundred and fortyone of these (91.1%) could be followed for ten years or until death. One hundred and twenty three patients (25.8%) experienced one or more adverse effects during the pharmacological treatment, and twenty five of these could be classified as serious. Fifty-seven malignancies were diagnosed during the observation time and three of these led to drug withdrawal (cervical cancer-infliximab, lymphoma-adalimumab and basalioma-azathioprine).

Surgery was performed in 16/330 UC and 33/154 CD patients. Frequency of early postoperative complications was 31% for UC patients and 36% for CD patients. Most complications were minor but two patients were re-operated, two needed intensive care unit and one patient died post-operatively.

	All IBD N=484	Ulcerative colitis N=330	Crohn's disease N=154
Salicylates, no. exposed	405 (83.7%)	305 (92.4%)	100 (64.9%)
Adverse effects	28	19	9
Sulphasalazine, no. exposed	104 (21.5%)	51 (15.5%)	53 (34.4%)
Adverse effects	27	12	15
Immunomodulators, no. exposed	210 (43.4%)	110 (33.3%)	100 (64.9%)
Adverse effects	53	29	24
Biologicals, no. exposed	71 (14.7%)	35 (10.6%)	36 (23.4%)
Adverse effects	17	8	9
Medical treatment overall			
Any medical treatment	476 (98.3%)	325 (98.5%)	151 (98.1%)
Total no. adverse effects	126	68	58
Total no. serious adverse effects	25	14	11
No. affected persons	123 (25.8%)	66 (20.3%)	57 (37.7%)
Any abdominal surgery	49 (10.1%)	16 (4.8%)	33 (21.4%)
Emergent surgery	17 (3.5%)	7 (43.8%)	10 (30.3%)
Cumulative complications			
No. surgical procedures	68	28	40
No. of complications	42	14	28
Pat with any complication	23	8	15

[Adverse effects of medical treatment and surgical complications]

Conclusion: Adverse effects related to medical therapy were experienced by approximately every fourth patients, and by every third patient that was operated.

Disclosure: Nothing to disclose

P0362

TREATMENT AND OUTCOME OF ULCERATIVE COLITIS DURING THE FIRST 10 YEARS AFTER DIAGNOSIS IN A PROSPECTIVELY FOLLOWED POPULATION-BASED COHORT

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Introduction: There is a shortage of studies evaluating the effect of prevalent use of immunomodulators and biologicals on the clinical course of ulcerative colitis during 10 years.

Aims & Methods: The aim of the present study is to report the use of drugs and surgery in a population based setting. Between 2005 and 2009 we identified 330 patients in all ages with a new diagnose of ulcerative colitis in the County of Uppsala in the middle of Sweden. They were followed prospectively and the medical notes have been scrutinized with special reference to the use of drugs and surgery.

Results: Out of the 330 patients, 297 (90.0%) could be followed for 10 years or until death. 23 patients died (7.0%) and 33 emigrated or rejected further contact. Three patients died as a consequence of the disease or its treatment. The cumulative exposition to drugs was as follows; 5-ASA 96.6%, steroids 73.3%, immunomodulators 35.4% and biologicals 11.4%. Fourteen patients (4.6%) were colectomized.

Severity at diagnosis

S1 190 (57.6%)

S2 126 (38.2%)

S3 14 (4.2%)

	First year	First five years	Ten years
5-ASA	90.4%	94.7%	96.6%
steroids	51.5%	64.4%	73.3%
IMM	11.8%	27.7%	35.4%
biologicals	2.5%	8.3%	11.4%
colectomy	1.2%	3.1%	4.6%

[Drug treatment and surgery, exposition to respective treatment]

Conclusion: Afrequent use of immunomodulators and biologicals with a continuing of start of new treatments during 10 years, resulted in a low need for colectomy without increased mortality.

Disclosure: Nothing to disclose

P0363

FREQUENCY OF HEREDITARY AND ACQUIRED THROMBOEMBOLIC COMPLICATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES IN MOSCOW

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Introduction: Thromboembolic complications (TC), which are one of the characteristic manifestations of inflammatory bowel diseases (IBD).

Aims & Methods: **Objective:** to identify the frequency of acquired and inherited hypercoagulation factors that contribute to the development of TC in patients with IBD. **Methods:** The clinical status of 1238 IBD patients undergoing treatment in 2019 was evaluated in the Department of IBD. 748 patients with ulcerative colitis (UC) and 490 patients with Crohn's disease (CD). In 112 patients with IBD (9.0%), clinically significant TC (venous thrombosis of the lower extremities, upper extremities and others) was detected. In patients with clinically significant feasibility studies, DNA isolated from peripheral blood lymphocytes was examined to identify molecular genetic mutations that lead to hypercoagulation.

Development of TC in patients with IBD.

Results: Of the 112 patients with TC, 76 (67.8%) patients had UC, and 36 (32.2 %) patients had Crohn's disease. Of 112 IBD patients with clinically significant TC, 45 (40.2 %) had genetic mutations that increase affinity for fibrinogen, increase platelet aggregation, disrupt folic acid metabolism, and reduce the activity of the methylenetetrahydrofolate reductase enzyme, which may be manifested by a moderate increase in homocysteine levels. 67 patients with IBD (59.8%) did not have genetic mutations that lead to hypercoagulation. Of the 45 IBD patients with clinically significant feasibility studies due to hereditary factors, 30 (66.6%) patients had UC, 15 (33.7%) patients had CD (HR-1.038, 95% CI 0.746-1.444; x²-0.049; p=0.83921).

Conclusion: Clinically significant feasibility studies were found in 9.0% of IBD patients. More than 40% of patients with clinically significant feasibility studies (n=112) have inherited factors that contribute to the development of feasibility studies. About 60 % of IBD patients with clinically significant feasibility studies do not have hereditary factors that lead to the development of feasibility studies.

Disclosure: Nothing to disclose

P0364

ESCHERICHIA COLI GENOTYPES AND BACTERIOCIN PRODUCTION IN THE LARGE BOWEL MUCOSA OF CROHN'S DISEASE AND ULCERATIVE COLITIS

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Introduction: Possible role of *Enterobacteriaceae* in the pathogenesis of inflammatory bowel disease has been studied substantially. It has been shown that a significant difference between mucosal bacteria (studied currently) and luminal ones (investigated in the past) exists. Four geno-

types of *Escherichia coli* strains are known: A and B1 which are usually associated with commensal strains; B2 and D genotypes, usually related to pathogenic strains for which more virulent factors are typical. These genotypes have been evaluated in colorectal neoplasia (1), nevertheless there is no data on their incidence and possible role in ulcerative colitis (UC) and Crohn's disease (CD). Bacteriocins (colicins and microcins) are proteins, produced by bacteria from the *Enterobacteriaceae* family. Bacteriocins possess antimicrobial, proapoptotic, probiotic and antineoplastic properties.

Aims & Methods: The aim of our prospective study was to assess whether there are differences in *Escherichia coli* genotypes and in bacteriocin production in the large bowel mucosa of CD and UC patients.

Mucosal biopsies were taken in the caecum, transverse colon and the rectum during the colonoscopy in patients with CD (29 biopsies; 10 patients; 4 men, 6 women; mean age 31+/-11) and UC (30 biopsies; 10 patients; 7 men, 3 women; mean age 45+/-13) after standardized bowel cleansing. Sterile disposable biopsy forceps were used for every single biopsy. Each biopsy specimen was immediately put into a transport liver-enriched broth. Culture on the blood and MacConkey agars followed. Isolated bacterial strains belonging to *Enterobacteriaceae* family were frozen at -80 °C. Subsequently, genotypes of *Escherichia coli* were investigated by PCR methods and bacteriocin production by bacteria from *Enterobacteriaceae* family was assessed by presence of zone of growth inhibition of the indicator strain and by PCR methods. All indicator strains were from in-house collection of strains (2).

Results: Fifty nine biopsy samples were investigated. A total of 32 *Escherichia coli* strains and 51 strains belonging to *Enterobacteriaceae* were cultured from 29 biopsies in CD patients. In total, 41 *Escherichia coli* strains and 54 strains belonging to *Enterobacteriaceae* family were obtained from 30 biopsies in UC patients. *Escherichia coli* genotype A1 was found in 25% CD and 17% UC patients; genotype B1 in 44% CD and 0% UC individuals; phylogroup B2 in 13% CD and 37% UC patients; genotype D in 18% CD and 46% UC individuals. Statistically significant difference in the frequency of *Escherichia coli* strains of genotype B1, B2 and D were found between CD and UC: p<0.001, p=0.031 and p=0.024. *Escherichia coli* of B2 or D phylogroup was present in 31% of CD biopsies and 83% UC biopsies which was of significant difference: p<0.001. In CD, colicin production was 18% (9/51), in UC 39% (21/54); p=0.019. Microcin production was in CD 12% (6/51), in UC 24% (13/54); p=0.130.

Conclusion: Our current study confirmed significant differences in genotypes of *Escherichia coli* and in colicin production in the large bowel mucosa of UC and CD. Particular genotypes of mucosal *Escherichia coli* and bacteriocins might play a role in different pathogenesis and distinct phenotypes of UC and CD.

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Disclosure: Nothing to disclose

P0365

THE ASSOCIATION BETWEEN PATIENT ACTIVATION AND HEALTH-RELATED QUALITY OF LIFE AMONG INDIVIDUALS WITH CROHN'S DISEASE

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Introduction: Patient activation refers to an individual's knowledge, skill, and confidence in managing their health. There is limited research demonstrating whether higher patient activation is associated with better health-related quality of life (HRQoL) among patients with Crohn's Disease (CD).

Aims & Methods: This study aimed to examine the association between patient activation level and HRQoL among US adults with CD. Data from Kantar's US 2017 National Health and Wellness Survey, an online self-administered survey, were analyzed. Adults were surveyed using stratified random sampling based on gender, age and race/ethnicity to ensure the sample was representative of the general adult population. Patient activation was measured using the Patient Activation Measure (PAM[®]), which measures patients on a 0-100 scale and segments patients into one of four activation levels with higher levels representing higher activation: L1: disengaged and overwhelmed; L2: becoming aware but still struggling, L3: taking control and gaining control, L4: maintaining behaviors and pushing further. Sociodemographics and comorbidities were also collected as covariates. HRQoL was assessed with Short-Form 36 health questionnaire version 2 (SF-36v2). Minimal important difference (MIDs) were defined as 3 points for mental component summary (MCS) and physical component summary (PCS) scores and 0.041 points for SF-6D health utilities index (derived from SF-36v2 items). Linear regression models were used to compare differences in HRQoL between PAM levels without post-hoc adjustment while controlling for covariates.

Results: Among 374 respondents with a self-reported physician diagnosis of CD, mean age was 49.4 years and 54.0% were male. A total of 23 respondents were PAM L1, 43 were L2, 175 were L3, and 133 were L4. The lowest PAM level was associated with younger age and having greater comorbidity burden. After controlling for covariates, patients with PAM L1 compared to patients with PAM L4 had significantly lower MCS scores (p=0.001) but did not have statistically significant differences on PCS scores (p=0.090). Other health domains which were significantly lower for L1 vs. L4 groups were general health, physical functioning, role physical, vitality, social functioning, role emotional, and mental health (all p≤0.05). SF-6D was also significantly lower for L1 compared with L4. Differences between L1 and L4 met MIDs for PCS, MCS, and SF-6D metrics. Significant differences were also found between L2 and L4 on general health (p=0.003) and vitality (p=0.019).

	PAM Level 1	PAM Level 2	PAM Level 3	PAM Level 4	P-value
	Mean	Mean	Mean	Mean	PAM 1 vs. 4
SF-36 MCS	35.70	41.90	42.40	42.6	.001
SF-36 PCS	37.30	40.20	39.30	40.7	.090
SF-6D Health Utilities Index	.55	.63	.62	.62	.01

[Table. HRQoL Adjusted Mean Scores by PAM level]

Conclusion: Lower patient activation was associated with poorer HRQoL. Individuals with CD who were at the highest level of activation had meaningfully higher HRQoL scores than individuals at the lowest level of activation. Future research should identify interventions which can improve levels of activation as it could potentially help reduce HRQoL impairments.

Disclosure: Eli Lilly provided funding for this analysis.

P0366

OCCURRENCE OF COLORECTAL CANCER AND THE EFFECT OF MEDICAL TREATMENT IN CROHN'S DISEASE PATIENTS

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Introduction: The risk of colorectal cancer (CRC) has previously been proven to be increased in both Ulcerative colitis and Crohn's disease (CD). Some studies have suggested that treatment with 5-aminosalicylates (5-ASA) has cancer preventive effects. However, only few studies have investigated the effect of monotherapy as well as combination therapy of immunomodulators and biological treatment on CRC development.

Aims & Methods: The aim was to estimate the relative risk of CRC development in a cohort of adult CD patients. All incident cases of CD (n=9,739) in the Danish National Patient Register between 1997 and 2015 were included. Cases were matched with up to 50 controls. Incident CRC cases after the index date were included from the Danish Cancer Registry. CD patients were divided into 6 subgroups due to medical treatment: none, systemic 5-ASA, immunomodulators, biologicals and two combined treatment groups: (1) 5-ASA and immunomodulators, 2) biologics and 5-ASA and/or immunomodulators. Cox regression and Kaplan-Meier estimates were used to investigate the association between CD and CRC development.

Results: The risk of CRC in CD patients compared to controls, was significantly higher with a HR of 1.43 (95% CI: 1.15-1.78) (p=0.001). CD patients in treatment with 5-ASA were in greater risk of developing CRC compared to those in the combined treatment group 2, with HR of 4.08 (95% CI: 1.30-12.79) (p=0.02). However, patients only receiving 5-ASA compounds were at a reduced risk of developing CRC compared to those with no medical treatment, HR 0.50 (95% CI: 0.27-0.92) (p=0.02).

Conclusion: The risk of developing CRC is significantly increased in patients suffering from CD compared to reference individuals. Medical treatment seems to have a preventive effect against CRC development and 5-ASA treatment alone is associated with lower risk of CRC compared to no medical treatment in CD patients.

Disclosure: Petra Weimers has received consulting fees from Ferring lægemidler and Tillotts Pharma AG

P0367 WITHDRAWN

P0368 WITHDRAWN

P0369

THE RISK OF LATER DEVELOPING INFLAMMATORY BOWEL DISEASE IN SUBJECTS WITH DERMATOLOGICAL DISORDERS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Dermatological conditions such as erythema nodosum (EN), pyoderma gangrenosum (PG), Sweet's syndrome and aphthous stomatitis can occur in association with inflammatory bowel disease (IBD).

Aims & Methods: A retrospective cohort study was performed among subjects without a prior IBD diagnosis, comparing those with any of the dermatological conditions associated with IBD to age/sex-matched controls. Hazard ratios (HR), assessing time to a subsequent diagnosis of IBD were adjusted for age, sex, body mass index, deprivation, comorbidity score, smoking status and the presence of diarrhoea, loperamide prescription, anaemia, lower gastrointestinal bleeding and abdominal pain. A logistic regression model was used to produce a prediction model for IBD diagnosis within three years of an EN diagnosis.

Results: 7,447 subjects with dermatological conditions (74% female, median age 38 (IQR 24-65) years) were matched to 29,297 controls. 131 (1.8%) IBD diagnoses in cases were observed compared to 65 (0.2%) in controls. The median time to IBD diagnosis was 205 (IQR 44-661) days compared to 1,594 (693-2,841) for controls ($p < 0.001$).

The adjusted HR for later developing IBD was 6.16 (95%CI 4.53-8.37), $p < 0.001$, while for UC the aHR was 3.30 (1.98-1.53), $p < 0.001$ and for CD 8.54 (5.74-12.70), $p < 0.001$. 5,590 EN subjects with 87 (1.6%) IBD diagnoses within 3-years were included in the prediction model development cohort. The model performed well with a bias-corrected c-statistic of 0.81 (95%CI 0.77-0.85).

Conclusion: Subjects with dermatological conditions associated with IBD have a six-fold increased risk of developing IBD. Younger age, smoking, low body mass index, anaemia and lower gastrointestinal symptoms increased the risk of IBD within 3 years.

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P0370

THE RISK OF LATER DEVELOPING INFLAMMATORY BOWEL DISEASE IN SUBJECTS WITH OPHTHALMIC DISORDERS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Ophthalmic conditions including uveitis, episcleritis and scleritis may occur in isolation or less commonly in association with the inflammatory bowel diseases (IBD) as extraintestinal manifestations.

Aims & Methods: A retrospective cohort study examined the risk of later developing IBD in those with an ophthalmic condition associated with IBD compared to age-sex matched controls. Hazard ratios (HR) for a subsequent diagnosis of IBD were adjusted for age, sex, body mass index, deprivation, comorbidity, smoking status and the presence of baseline axial arthropathy, diarrhoea, loperamide prescription, anaemia, lower gastrointestinal bleeding and abdominal pain. A prediction model for the risk of developing IBD within three years of a uveitis diagnosis was developed using multivariable logistic regression analysis.

Results: 39,402 subjects with an ophthalmic condition associated with IBD were identified (median age 51 (38-65), 57% female) and matched to 155,361 controls. 218 (0.6%) IBD diagnoses (108 UC and 115 CD) were observed in cases and 339 (0.2%) (223 UC and 116 CD) in controls. The median time to an IBD diagnosis was 905 (IQR 381-2,166) days and 1,403 (611-2,516) in controls ($p < 0.001$). Following adjustment, ophthalmic conditions associated with IBD carried a Hazard Ratio of 2.22 for IBD (95%CI 1.87-2.64), 1.61 (1.27-2.04) for ulcerative colitis and 3.41 (2.62-4.43) for Crohn's disease, all p -values < 0.001 . Within 3-years of a uveitis diagnosis 84 (0.4%) subjects had a recorded diagnosis of IBD. The prediction model performed well with a c-statistic of 0.74 (95%CI 0.70-0.81).

Conclusion: Subjects with ophthalmic conditions associated with IBD have a two-fold increased risk of developing IBD. Lower gastrointestinal bleeding, age 18-30 year olds, diarrhoea and anaemia were strong predictors of later developing IBD in those with a new uveitis diagnosis.

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P0371

MANAGEMENT OF PATIENTS NEWLY DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE BASED ON HOSPITAL CHARACTERISTICS: RESULTS FROM THE NATIONWIDE EPIDEMIBD STUDY OF GETECCU

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Introduction: Updated information on the treatment of inflammatory bowel disease (IBD) in Europe based on hospital characteristics is lacking.

Aims & Methods: Our aim was to examine the use of drug treatments, surgery and hospitalisations in newly diagnosed IBD patients in the biological era based on hospital characteristics. Prospective and population-based

nationwide registry. Adult patients diagnosed with IBD -Crohn's disease (CD), ulcerative colitis (UC) or IBD unclassified (IBD-U)- during 2017 in all the 17 Spanish administrative regions were included. Hospitals were classified, according information provided by the Spanish Ministry of Health, into five categories: 1) Small general hospitals (less than 150 beds on average, hardly any high-tech resources, low patient-complexity); 2) Medium general hospitals (average size less than 200 beds, minimal technological resources some teaching activity and more complexity attended); 3) General hospitals (of average size around 500 beds, medium patient-complexity); 4) Referral hospitals (large hospitals but heterogeneous in endowment, size and activity, high teaching activity and patient-complexity); and 5) Large referral hospitals (great structural weight). Hospitals from groups 1 and 2 were considered with low resources (LR) and from groups 3-5 hospital with high resources (HR). The Kaplan-Meier method was used to estimate the time course of the use of treatments, surgery, and hospital admissions and, with differences assessed with the log-rank test.

Results: The study cohort comprises 3,611 incident cases of IBD diagnosed during 2017 in 108 hospitals covering over 22 million adult inhabitants (about 50% of the Spanish population). One-hundred seventy seven patients were treated in hospitals with LR (n=6) and 3,434 patients in HR hospitals (n=102). The main characteristics of IBD patients (including IBD type, phenotype or disease extension) were similar between both groups. The cumulative incidence of mesalamine treatment in CD was significantly higher in LR hospitals, while treatment with systemic steroids was higher in hospitals with HR (mainly due to higher proportion of patients starting systemic steroids at IBD diagnosis) (table 1). In addition, the exposure to biologics was also higher in CD patients from HR hospitals. The cumulative incidence of surgery and hospitalizations was similar in both groups. Regarding UC, the cumulative incidence of treatment with mesalamine, steroids, immunomodulators, biologics and surgery was similar in hospitals with LR and those with HR.

Conclusion: In the EpidemIBD cohort, the use of biological agents is much higher than previously reported, mainly in CD patients and in hospitals with HR. The use of drugs was different in CD patients based on hospital characteristics (higher use of steroids and biologics in HR centers). Nevertheless, the benefit of more frequent use of biological drugs in the natural history of the disease must be demonstrated.

Treatments	Type of hospital	Cumulative incidence of exposure during follow up (%)				
		3 months	6 months	9 months	12 months	p-value
Mesalamine	LR hospitals		43	52	52	0.003
Mesalamine	HR hospitals		32	35	36	0.003
Systemic steroids	LR hospitals		27	28	30	0.01
Systemic steroids	HR hospitals		40	43	44	0.01
Immunomodulators	LR hospitals		29	42	46	0.7
Immunomodulators	HR hospitals		31	41	46	0.7
Biologics	LR hospitals		5	8	12	0.03
Biologics	HR hospitals		13	19	24	0.03
Surgery	LR hospitals		4	4	7	0.5
Surgery	HR hospitals		7	9	10	0.5

[Table 1. Cumulative incidence of exposure of Crohn's disease patients to therapeutic choices based on hospital type.]

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P0372

PREGNANCY COMPLICATIONS IN WOMEN WITH INFLAMMATORY BOWEL DISEASE: A NATIONAL COHORT STUDY

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Introduction: Previous studies have been inconsistent in regard to the risk of pregnancy-related complications in women with IBD.

Aims & Methods: This was a nationwide case-control study using the 2014 USA National Inpatient Sample (NIS) to measure the frequency of an ICD9 code for a pregnancy complication in women with IBD versus no IBD. Pregnancy complications included spontaneous abortion, post abortion complications, ectopic pregnancy, hemorrhage, hypertensive disorders, early labor, polyhydramnios, prolonged pregnancy, gestational diabetes, fetal distress, umbilical cord complications, obstetric trauma, hyperemesis, missed abortion, mental disorder during pregnancy, forceps delivery, infections and anemia. We performed univariate and multivariate logistic regression controlling for confounders predisposing to pregnancy complications including antiphospholipid syndrome, SLE, hyperthyroidism, hypothyroidism, chlamydia, gonorrhea and cervical incompetence.

Pregnancy complication	IBD Frequencies N=6705 (0.21%)	Non-IBD Frequencies N=3255890 (99.79%)	P value univariate	OR (95%CI)	P value multi- variate
Infectious and parasitic complications	505 (7.53%)	145365 (4.46%)	<0.0001	1.64 (1.33-2.02)	<0.0001
Anemia	300 (4.47%)	28735 (0.88%)	<0.0001	5.69 (4.15-7.80)	<0.0001
Infections of genitourinary tract	115 (1.71%)	38125 (1.17%)	0.06	1.65 (1.07-2.60)	0.02
Hypertension	665 (9.92%)	372580 (11.44%)	0.09	0.80 (0.62-0.92)	0.005
Preeclampsia	115 (1.71%)	79225 (2.43%)	0.09	0.62 (0.40-0.97)	0.04
Obstetric trauma	1945 (29%)	1269505 (39%)	<0.001	0.63 (0.55-0.71)	<0.001
Prolonged pregnancy	515 (7.68%)	448065 (13.76%)	<0.0001	0.50 (0.41-0.62)	<0.0001
Gestational diabetes	395 (5.89%)	256075 (7.86%)	0.0092	0.68 (0.53-0.87)	0.0023
Fetal distress	370 (5.52%)	317200 (9.74%)	<0.0001	0.57 (0.45-0.74)	<0.0001
Umbilical cord complications	1170 (17.45%)	727585 (22.34%)	<0.0001	0.72 (0.63-0.84)	<0.0001

Model variables: age, race, mortality risk, income, hospital location, hospital size, insurance, SLE, hyperthyroidism, hypothyroidism and cervical incompetence.

[Summary of statistically significant pregnancy complications. Univariate analysis and adjusted odds ratios predicting pregnancy complications in IBD]

Results: 3262595 women ages 18-35 were discharged on 2014 with a pregnancy complication. From this cohort, 6705 (0.21%) had IBD. The mean age for cases and controls was 29 and 27 years respectively. Cases were more likely to be Caucasian (78% vs 54%) and be admitted to urban academic hospitals along with a slightly higher mortality risk.

In multivariate analyses, there was no statistically significant difference ($p>0.05$) between cases and controls for: spontaneous abortion, post abortion complications, ectopic pregnancy, hemorrhage, severe preeclampsia, eclampsia, early labor, polyhydramnios, hyperemesis, missed abortion, mental disorder during pregnancy and forceps delivery.

When compared to women with no IBD, women with IBD had significant lower odds for prolonged pregnancy, gestational diabetes, fetal distress, umbilical cord complications, obstetric trauma, mild preeclampsia and hypertension. There was, however, higher odds for infectious and parasitic complications (OR 1.74 95%CI 1.42-2.14, $p<0.0001$), UTIs (OR 1.65 95%CI 1.07-2.60 $p=0.02$) and anemia (OR 5.26 95%CI 4.01-6.90 $p<0.0001$).

Conclusion: In this large nested case-control study, women with IBD did not have a higher risk of common pregnancy complications compared to non-IBD mothers. There was a higher risk for infection and anemia, likely secondary to immunosuppressive medications for treatment and the disease itself. These data are important to share with women with IBD considering pregnancy.

Disclosure: Nothing to disclose

P0373

NATURAL HISTORY OF RECURRENT CROHN'S DISEASE FOLLOWING ILEOCOLONIC RESECTION: A MULTICENTER RETROSPECTIVE CROSS-SECTIONAL COHORT STUDY

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Introduction: Postoperative recurrence remains a frequently observed problem in patients with Crohn's disease (CD). Prediction of post-operative recurrence (POR) based on clinical risk factors alone has thus far been inconclusive and prophylactically treating clinically high-risk patients is based on limited evidence.

Aims & Methods: This study aimed to assess the natural history of CD following ileocolonic resection unbiased by post-operative treatment, identify risk factors of endoscopic recurrence and examine the association between clinically high- and low-risk patients in developing endoscopic recurrence.

Medical records of 142 patients with established CD at the Amsterdam University Medical Center (the Netherlands), UZ Gent (Belgium) and University Medical Center Ljubljana (Slovenia) receiving follow-up for ileocolonic resection without post-operative IBD medication were reviewed. Baseline characteristics and clinical phenotypic data were retrospectively extracted. Endoscopic recurrence was defined as a Rutgeerts score $\geq 2b$, using detailed endoscopy reports and images, reviewed by a single expert gastroenterologist. Clinically high-risk patients were defined as having 1 or more of the following risk factors: smoking, prior intestinal surgery, penetrating disease at index surgery, perianal location and granulomas in re-

section specimen.¹ For a subset of patients (N= 95) all resection specimens were reviewed for the presence of granulomas by a single IBD pathologist. Both uni- and multivariate logistic regression analysis was performed to identify possible risk factors for endoscopic recurrence and assess the relationship between high- and low-risk profiles and endoscopic recurrence. **Results:** Overall endoscopic recurrence was observed in 46.5% of patients ($\geq 2b$) and 67.7% ($\geq 2c$).

Univariate analysis showed active smoking both 1 year prior to (OR 2.26, $p=0.04$) and 1 year following surgery (OR 3.66, $p=0.004$), age at surgery (OR 1.03, $p=0.04$), Montreal classification A3 (OR 4.05, $p=0.006$) and the amount of previous IBD-related bowel resections (OR 1.88, $p=0.03$) to be independently associated with endoscopic recurrence. After multivariate analysis, active smoking 1 year following surgery (OR 3.33, $p=0.01$), Montreal classification A3 (OR 3.32, $p=0.03$) and the number of previous IBD-related bowel resections (OR 2.00, $p=0.03$) remained significantly associated with endoscopic recurrence.

No significant association with endoscopic recurrence was observed between patients in the high- vs the low-risk group (OR 1.18, $p=0.70$). Having 3 or more risk factors compared to less than 3 resulted in a significant increased odds of developing endoscopic recurrence (OR 3.48, $p=0.03$). Comparing 3 or more risk factors including at least active smoking resulted in a higher increased odds for developing endoscopic recurrence (OR 3.84, $p=0.05$) illustrating its relative importance as a clinical risk factor.

Conclusion: Overall endoscopic recurrence using the modified Rutgeerts score without therapeutical interference is seen in 46.5% of patients within 3-12 months following surgery. Active smoking 1 year following surgery, Montreal classification A3 and previous IBD resections were identified as risk factors for post-operative endoscopic recurrence within this cohort. We observed no difference in clinically high- vs low-risk patients yet having 3 or more risk factors, with or without active smoking, resulted in a significant increased odds of developing endoscopic recurrence. This subgroup might benefit from early post-operative prophylactic treatment.

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P0374

DIETARY INTAKE IS ASSOCIATED WITH FLARE DEVELOPMENT IN IBD PATIENTS

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Introduction: Diet is often considered to play a (pivotal) role in onset and progression of inflammatory bowel disease (IBD). 33-57% of the IBD patients believe that diet might contribute to the development of a flare.

However, studies on this topic are sparse. Hence, we aimed to analyse the association of dietary patterns with the development of flares in a longitudinal study in two geographically distinct IBD cohorts in the Netherlands.

Aims & Methods: In both cohorts, Crohn's disease (CD) and ulcerative colitis (UC) consecutive patients were included and followed for two years. A flare was defined by either 1) endoscopy or radiology 2) faecal calprotectin ($> 250 \mu\text{g/g}$ or >100 with at least five-fold increase from the previous visit) and/or 3) treatment adjustment in combination with clinical symptoms or CRP above hospital cut-off. Baseline characteristics between the cohorts were analysed by a student's t-test or χ^2 -test when appropriate. Habitual dietary intake was obtained via semi-quantified food frequency questionnaires. Principal-components analysis (PCA, varimax rotation) was conducted on the entire cohort to identify relevant dietary patterns as derived from 22 food groups. To evaluate if these patterns were associated with development of a flare, a COX proportional hazards analysis was performed among patients in remission at baseline and adjusted for several covariates.

Results: In this study, a total of 724 IBD patients were included: 486 patients (284 CD, 202 UC) from the northern cohort and 238 patients (156 CD, 82 UC) from the southern cohort. Compared to the Southern cohort, patients in the Northern cohort were significantly younger at diagnosis, less likely men and had lower energy intakes.

Prior to analysis, the suitability of the PCA was confirmed by the overall Kaiser-Meyer-Olkin (KMO) of 0.655 and Bartlett's Test of Sphericity being statistically significant ($p<0.001$), indicating that the data was likely factorizable. Based on visual inspection of the scree plot and interpretability criteria, 3 dietary patterns were retained, explaining 11.6%, 8.9% and 8.3% respectively (cumulative 28.8%) of the total variance. The first pattern is characterized by intake of grain products, cooking oils and fats, potatoes, processed and red meat, condiments and sauces, and sugar, cakes and confectionery; the second by processed and red meat, condiments and sauces, alcoholic beverages, coffee, snacks, and negatively loaded by tea and fruits; and the third by fruits, fish, eggs, vegetables, nuts and seeds, alcoholic beverages, and negatively loaded by non-alcoholic beverages.

Of the 724 included patients, 428 were in remission at baseline and eligible for the COX proportional hazard analysis. Of those patients, 107 developed (25.0%) a flare during follow-up. In the COX proportional hazard analysis (correcting for kilocalories, cohort, gender, disease phenotype, BMI, age at diagnosis and active smoking status), the first dietary pattern (HR: 1.520, 95% CI: 1.053-2.195, $p=0.026$) was associated with increased risk of flare development, as was being female (HR 1.584, 95% CI 1.017-2.466, $p=0.042$).

Conclusion: Adherence to a dietary pattern characterized by intake of grains, oils, potatoes, processed and red meat, condiments and confectionery which could be regarded as a "traditional Dutch" pattern is associated with development of a flare. Further research is needed to confirm this association.

References: VP and CS share first author, MC and DJ share last author.

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P0375

PATIENTS WITH INFLAMMATORY BOWEL DISEASE ARE AT AN INCREASED RISK OF ACUTE PANCREATITIS: A POPULATION-BASED STUDY

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Introduction: There is paucity of large population-based studies addressing the relationship between acute pancreatitis (AP) and inflammatory bowel disease (IBD).

Aims & Methods: The aim of this study was to hypothesize an increased risk of AP after a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC). Secondly, we aimed to look at the effect of various classes of IBD medications on this proposed increased risk. This study was conducted using the IBM Explorys Database to extract de-identified aggregated patient health records accumulated from May 2015 to May 2020. Data was obtained using the Systematized Nomenclature of Medicine-Clinical Terms (SNOMED-CT) criteria with search terms for Crohn's disease, ulcerative colitis, and subsequent acute pancreatitis utilizing a temporal relationship. IBD medications were divided into groups based on the class of medication as follows: (1) 5-aminosalicylic acid drugs (5ASA), (2) purine analogues, (3) glucocorticosteroids (GCS), and (4) biologics/immunomodulators. We reported odds ratios (OR) with 95% confidence intervals (CI) where $P < 0.05$ was considered statistically significant.

Results: Explorys identified 39,514,140 unique electronic medical records during the study period. A total of 169,600 patients had a diagnosis of CD and 134,370 had a diagnosis of UC. In both cohorts, we report a higher proportion of females and patients < 60 years of age who developed subsequent AP ($P < 0.05$). Overall, both CD and UC patients had a higher OR of developing AP when compared to the control population who did not have CD (OR 4.41; 95% CI 4.28 - 4.54; $P < 0.05$) or UC (OR 3.93; 95% CI 3.80 - 4.08; $P < 0.05$). The prevalence of AP in the CD population was significantly higher versus the UC population (2.69% vs 2.40% $P < 0.05$). The role of IBD-medications in both CD and UC cohorts resulted in an overall lower risk of AP versus the overall cohorts (**Table 1**).

	CD (OR, 95% CI, P)	UC (OR, 95% CI, P)
Overall	4.41, 4.28 - 4.54, $P < 0.0001$	3.93, 3.80 - 4.08, $P < 0.0001$
Treated with 5ASA	1.17, 1.10 - 1.25, $P < 0.0001$	1.02, 0.96 - 1.10, $P = 0.4608$
Treated with purines	1.20, 1.11 - 1.30, $P < 0.0001$	1.20, 1.08 - 1.33, $P = 0.001$
Treated with GCS	1.40, 1.31 - 1.46, $P < 0.0001$	1.37, 1.28 - 1.46, $P < 0.0001$
Treated with biologics or Immunomodulators	1.45, 1.38 - 1.53, $P < 0.0001$	1.55, 1.46 - 1.66, $P < 0.0001$

[Odds ratios (OR) for developing Acute Pancreatitis]

Conclusion: Patients with CD or UC have an increased risk of developing AP when compared to patients without CD or UC. IBD associated medications (such as GCS and purine analogs) in themselves are linked to AP and continued to pose an increased risk of AP in our study, this risk however was significantly lower than that in the overall IBD cohorts. These findings suggest that controlling inflammation can reduce the risk of AP in IBD patients.

Disclosure: Nothing to disclose

P0376

RISK FACTORS ASSOCIATED WITH FAMILIAL INFLAMMATORY BOWEL DISEASE - A DANISH NATIONWIDE STUDY

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Introduction: A positive family history of inflammatory bowel disease (IBD) is the strongest risk factor for subsequently developing disease. Nevertheless, despite sharing genetics and the same environment, some first-degree relatives (FDRs) will develop IBD, while others will not. Herein, we analysed FDRs of IBD probands in order to identify risk factors associated with the development of IBD.

Aims & Methods: A nationwide case-control study using the Danish National Patient Register, from January 1977 to December 2018. The inclusion criteria were families with at least two FDRs with IBD (at least one parent and one child). Cases were defined as FDR within these IBD-families diagnosed with IBD. Controls were FDR within these IBD-families not diagnosed with IBD. All exposures were defined using the Danish National Patient Register from 1977 onwards, except for antibiotics and mode of delivery where data was only available after 1995. Variables studied included sex, birth order, mode of delivery, personal and family history of immune-mediated diseases, gastroenteritis and surgical history preceding diagnosis. Cases and controls were compared within the family using uni- and multivariate conditional logistic regression.

Results: Overall, 4,179 individuals within 1,669 families were included, corresponding to 2,447 cases and 1,732 controls. Mothers were more frequently the parental case of IBD within the family (cases: 52.8%; controls 53.4%). The median (p25; p75) age of IBD diagnosis in mothers was 47.6 (35.3; 59.1), in fathers 51.7 (38.2; 62.9) and in children 26.1 (19.6; 34.2) years. There was a median (25p; 75p) of two (2; 3) children per family. In univariate analysis, being born a female (OR 1.40 95% CI [1.23-1.59]), having a history of immune-mediated diseases (OR: 1.35, 95% CI 1.00, 1.83), and receiving antibiotic treatment (OR 1.29, 95% CI [1.03-1.61]) were associated with a higher risk of IBD. In multivariate analysis, this effect persisted (female gender (aOR 1.40, 95% CI [1.23-1.59]); antibiotic treatment (OR 1.28, 95% CI [1.02-1.62])). Furthermore, ankylosing spondylitis was associated with an increased risk (aOR 2.88, 95% CI [1.05-7.91]) for disease development. Birth order, mode of delivery, appendectomy, tonsillectomy, asthma, depression and other immune-diseases were not associated with a higher risk for IBD.

Conclusion: In FDR's of IBD patients, female gender, history of ankylosing spondylitis and antibiotic treatment were associated with a higher risk for IBD development. These results offer an opportunity for counselling IBD families, and at the same time help to identify people at higher risk for developing disease who could be further studied for disease development.

Disclosure: Nothing to disclose

P0377

THE INCREMENTAL RATE OF THROMBOEMBOLIC EVENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE COMPARED TO PATIENTS WITHOUT IMMUNE-MEDIATED DISEASES

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Introduction: Inflammatory bowel diseases (IBD) have been associated with a higher risk of thromboembolic events, possibly due to the link between systemic inflammation and hypercoagulability. As the management of IBD has changed dramatically and several novel IBD therapeutic agents have been approved, there is a need to systematically assess the association between IBD and thromboembolic events in the current era. Such an assessment will also serve as a baseline reference for newer agents for IBD, such as JAK inhibitors.

Aims & Methods: This was a retrospective cohort study. Adult patients with IBD (≥ 2 diagnoses for IBD) were identified from the IBM MarketScan Commercial and Medicare-Supplemental Claims database (2014-2018) and matched 1:1 on age, sex, and index year to patients without any immune-mediated diseases (IMD). Data collected included demographics, comorbidities, and medications. The primary outcome was the development of a thromboembolic event (venous: deep vein thrombosis [DVT] and pulmonary embolism [PE]; arterial: myocardial infarction [MI] and ischemic stroke [IS]). To include patients at various stages of IBD disease severity, the index date was the day after a randomly selected IBD medical claim for patients with IBD, and the day after a randomly selected medical claim for patients without IMD. The baseline period was 1-year period prior to the index date, and the study period was the period from index to earliest of date of death, end of continuous insurance eligibility, or end of data (up to 4 years). Incidence rates (IRs) of thromboembolic events during the study period were calculated for each cohort. Unadjusted and adjusted incidence rate ratios (IRRs) from generalized estimating equations were used to compare cohorts. Adjusted IRRs controlled for age, sex, baseline comorbidities, baseline medications excluding those for IBD treatment, and baseline thromboembolic event of interest.

Results:

A total of 34,687 matched pairs (mean age 49.0 years, 54.4% female) were included. Patients with IBD generally had higher proportions of comorbidities compared to patients without IMD (e.g., Charlson comorbidity index [0.7 v 0.4]; cardiovascular disease [44.6% v 42.2%]; both $p < 0.0001$). A significantly higher proportion of patients with IBD experienced a baseline thromboembolic event compared to patients without IMD (4.7% v 2.6%, $p < 0.0001$). Unadjusted IRs of any thromboembolic event were 0.192 and 0.094 per person-year during the study period for patients with IBD and without IMD, respectively. In both the unadjusted and adjusted analyses, patients with IBD experienced higher rates of venous thromboembolic events compared to patients without IMD (Table 1: adjusted IRRs: 2.44 for DVT, 1.90 for PE; both $p < 0.0001$). Such increased rates were not observed for the arterial events (Table 1: adjusted IRRs: 1.15 for IS, 0.62 for MI).

Conclusion: Patients with IBD had significantly increased rates of DVT and PE compared to patients without IMD. Increased rates were not observed for IS and MI. The potential association between recent novel IBD therapies and increasing risk of venous thromboembolic events needs further investigation. Moreover, this elevated risk should be carefully considered when selecting treatment options that may further exacerbate this risk.

	Unadjusted IRR of IBD vs. without IMD (95% CI)	P-value	Adjusted IRR of IBD vs. without IMD (95% CI)	P-value
Thromboembolic event (any)	2.04 (1.78, 2.34)	<0.0001	1.49 (1.30, 1.71)	<0.0001
IS	1.32 (1.03, 1.69)	0.026	1.15 (0.89, 1.50)	0.278
MI	0.81 (0.59, 1.11)	0.187	0.62 (0.44, 0.88)	0.008
DVT	3.75 (3.02, 4.64)	<0.0001	2.44 (2.00, 2.99)	<0.0001
PE	3.15 (2.34, 4.24)	<0.0001	1.90 (1.42, 2.54)	<0.0001

[Table 1: Adjusted and unadjusted incidence rates of thromboembolic events in patients with IBD versus a population without IMD]

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P0378

ASSESSMENT OF COMORBIDITY AND PHYSICAL CAPACITY AS MARKERS FOR SAFETY OUTCOMES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: World-wide, the incidence and prevalence of inflammatory bowel diseases (IBD) increases in the older patient population. Previously published literature on adverse health outcomes in older patients has focused on patient age as a potential risk factor. However, age is an imperfect marker of the reduced physiological reserve that predisposes these patients to adverse health outcomes.

Aims & Methods: To assess how patient age, comorbidity and physical capacity are associated with hospitalisations and complications during hospitalisation after follow-up in older and adult IBD patients. Consecutive older (aged ≥ 65 years) and adult (aged 18 to 64 years) IBD patients were prospectively included at a tertiary referral centre. At baseline, clinical disease activity was measured using the Harvey Bradshaw Index (Crohn's disease; active disease >4 points) and partial Mayo score (Ulcerative Colitis or IBD-Unclassified; active disease >2 points). Comorbidity was measured using the Charlson Comorbidity Index (CCI) [1] and physical capacity with a hand dynamometer assessing hand grip strength, corrected for Body Mass Index and sex. [2]

After 18 months follow-up, the number of hospitalisations was recorded through screening of the electronic medical record. The first hospitalisation after baseline was used to assess if complications occurred during or after hospitalisation. Complications were defined as one of the following events: need for intercollegiate consultation, delirium, infection, fall, blood or iron transfusion, surgery, pressure ulcers, re-admission within 30 days after discharge or mortality. For both outcomes a logistic regression model was used in which age group, the CCI, impaired physical capacity

ity, sex, IBD type and clinical disease activity were entered if p-value had reached < .200 in univariate analyses. A p-value of < .050 was considered statistically significant.

Results: In total, 333 patients (174 older and 159 adult) were included, median age 70 (IQR 67-73) and 41 (IQR 29-51), percentage remission at baseline 82% and 70%, respectively. Sixty-seven (39%) patients had one or more comorbidities in the older patient group, compared to 23 (14%) in the adult group. Impaired physical capacity was present in 24 (14%) and 9 (6%) patients. Forty-three hospitalisations occurred in older patients, compared to 34 in adult patients, $p=.472$. Seventeen (40%) and 23 (68%) hospitalisations were IBD-related, $p=.014$. Twenty-three (30%) first hospitalisations had one or more complications. The CCI was independently associated with one or more hospitalisations during follow-up (OR 1.558, 95% CI 1.226-1.981, $p<.001$). In patients hospitalized during follow-up, impaired physical capacity was independently associated with a complicated course of the first hospitalization (OR 6.599, 95% CI 1.154-37.735, $p=.034$). Age was not associated with hospitalisation or complications during first hospitalisation.

Conclusion: The number of hospitalizations did not differ between older and adult IBD patients, however, older patients were less often hospitalised due to an IBD-related cause. Age was not associated with the occurrence of hospitalisations or complications. However, we found that the presence of comorbidities was associated with hospitalisation and impaired physical capacity with a complication during first hospitalisation. Therefore, this study establishes the importance of assessing comorbidities and physical capacity in IBD care and research, rather than focussing on age alone.

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Disclosure: Nothing to disclose

P0379

BIO-NAIVE CROHN'S DISEASE PATIENTS WITH LONG-STANDING DISEASE BENEFIT FROM USTEKINUMAB TREATMENT: REAL WORLD EXPERIENCE

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Introduction: Ustekinumab (UST) is a human anti-IL12/23 p40 monoclonal antibody, approved for treatment of Crohn's Disease (CD). This multicenter, non-interventional, retrospective chart review explored robust real-life data in patients receiving UST to access long-term efficacy and treatment persistence of UST treatment in the bio-naive CD population with long-standing disease.

Aims & Methods: Clinical data, such as maintenance of clinical response using Harvey-Bradshaw index, combined steroid-free and biochemical clinical remission, endoscopic response/healing via the simple endoscopic score for Crohn's disease (SES-CD), dose escalation and treatment persistence were assessed in 42 adult patients (55% female; mean age 46 ± 15.1 years; mean BMI 25.28 ± 4.5 kg/m²) with long-standing (mean

duration of 10,5 years) biologic-naive CD from 3 tertiary centers (one Slovenian and two Croatian) between January 2018 and April 2020. Data were collected before first infusion, at week (W)24, W52, as well as last follow-up.

Results: At W24 84% (35/42) of CD patients had achieved clinical response and 38.1% (16/42) were in combined steroid-free and biochemical clinical remission. After an average of 16 months of treatment duration, 88.1% (37/42) of CD patients were still on UST treatment, 71.4% (30/42) had maintained clinical response and 35.7% (15/42) were in sustained steroid-free clinical remission. The number of patients requiring steroid treatment was reduced by 87%. Mean HBI decreased from 8 to 3 and SES-CD from 6 to 2. The majority [59.53%] of patients started ustekinumab as monotherapy, i.e. without concomitant immunomodulator medication. 31% of patients experienced UST dose escalation.

Conclusion: UST offers an effective and persistent steroid sparing treatment option in this real-life multicenter study of bio-naive CD patients with long-standing disease.

Disclosure: Nothing to disclose

P0380

DEEP ENDOSCOPIC ULCERATIONS ARE NOT ASSOCIATED WITH THE NEED FOR SURGERY OR COMPLICATED BEHAVIOR: A POPULATION-BASED STUDY

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Introduction: Severe endoscopic lesions (SEL) during Crohn's disease (CD) are usually thought to increase disease complications and the need for surgery but based on a low level of evidence. Aims were to assess disease outcomes of patients with SEL at CD diagnosis on a population-based cohort.

Aims & Methods: All incident cases of CD were prospectively registered from 1994 to 1997 in Brittany, France. All charts of patients were reviewed from the diagnosis to the last clinic in 2015. Patients with stricturing or fistulizing disease at diagnosis were excluded. Endoscopic features were recorded according to the items of the CDEIS at diagnostic. SEL were defined by a deep ulceration on at least one intestinal segment. Bowel damage was defined according to the criteria that weight the Lemann Score (surgery, penetrating complications, anoperineal involvement). Survival analysis was performed to assess the association between SEL and disease outcomes (surgery, bowel damage, hospitalization for disease flare and immunosuppressant initiation).

Results: Among the 272 cases followed-up patients, 164 patients were included (exclusion of 96 (35%) patients for stricture or fistula at diagnosis and 14 (5%) for incomplete colonoscopy). There were 90 (55%) males. According to the Montreal classification 93 patients (57%) were A2 and the disease location was L1, L2 and L3 for 16 (10%), 70 (43%) and 77 (47%) of patients, respectively. Deep ulcers were present at initial colonoscopy for 41 (25%) patients on at least one segment, on two segments for 21 (13%) patients. The 41 patients presenting with SEL were more likely hospitalized ($p=0.03$) with a weight loss history ($p=0.04$). Patients with extended deep ulcerations on at least two segments were in addition more often smokers ($p=0.01$). With a mean follow-up of 12,3 years, the cumulative probabilities at 10 years of developing bowel damage, for the need of surgery, hospitalization and immunosuppressant were 40%, 21 %, 34% and 36%, respectively. There were no association between the presence of SEL

and the need for surgery (log rang=0.19) nor the onset of bowel damage (log rang=0.69). However, patients with SEL were more likely hospitalized (log rang=0.04) and more likely treated with an immunosuppressant (including anti-TNF) (log rang =0.0036). Conversely, immunosuppressant intake was associated with an increased need for surgery and the onset of bowel damage even when analysis were restricted to the initiation of an immunosuppressant before each outcome.

Conclusion: On a population-based cohort of Crohn's disease patients, SEL at diagnosis are associated with a more severe clinical disease but not with an increased risk of surgery nor bowel damage on the long-term despite an increased use of immunosuppressant.

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P0381

RISK OF PREVALENT ASTHMA AMONG CHILDREN AFFECTED BY INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED BIRTH COHORT STUDY

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Introduction: Inflammatory bowel disease (IBD) and asthma are two relevant and very impactful immune-mediated diseases that share common genetic and environmental risk factors. To the best of our knowledge, past studies have not thoroughly investigated differences in the risk of co-occurrence of childhood onset IBD and asthma, especially in relation to gender and specific age at IBD onset. Furthermore, results in literature regarding this association are discordant

Aims & Methods: The aim of this study is to analyze the risk of prevalent asthma among children affected by IBD in a population-based birth cohort, stratifying by sex, type of IBD (Crohn's disease and ulcerative colitis) and age at IBD onset, focusing especially on Very Early-Onset IBD (VEO-IBD).

The study population consisted of all children born between 1989 and 2012 in the region of Friuli-Venezia Giulia (North-eastern Italy). A nested matched case-control design on a longitudinal cohort of 213,515 newborns was adopted. Conditional binomial regression models were used to estimate Odds Ratios (OR) and 95% confidence intervals (CI) of asthma among children with IBD compared to controls. Analyses were stratified by sex, type of IBD (Crohn's disease and ulcerative colitis) and the age at IBD onset, in particular IBD children were categorized in three groups: Pediatric IBD between 10 and 17 years (Paris classification A1b); Early-onset (EO)-IBD between 0 and 9 years (Paris classification A1a); VEO-IBD between 0 and 5 years

Results: We observed 162 children with IBD and 1620 controls. The risk of being affected by asthma was higher among subjects with any type of IBD (OR: 1.49 95% CI 1.05-2.12), with a significantly increased risk only for males (OR: 1.60 95% CI 1.02-2.51). Among the 56 children with IBD and asthma, 47 (83.9%) had been diagnosed with asthma before IBD onset. Prevalence of asthma appeared to be increased in children affected by Crohn's diseases (OR: 1.29 95% CI 0.78-2.14) or ulcerative colitis (OR: 1.59 95% CI 0.92-2.74) compared to references, although results failed to attain statistical significance. When stratifying by age at IBD onset, younger age was associated with higher risks of asthma. Children with VEO-IBD had a marked increased risk of asthma (OR: 2.75 95% CI 1.26-6.02), while these estimates, were progressively lower and did not reach statistical significance for children with EO-IBD (OR: 1.70 95% CI 0.95-3.05) and Pediatric IBD (OR: 1.39 95% CI 0.90-2.15).

Conclusion: This study has found an elevated variability in the risk of co-occurrence of asthma across children affected by different types of IBD. Male children and patients with VEO-IBD are more likely to be affected by asthma at some point in their childhood. Our results suggest that it may be worth providing specific attention for respiratory symptoms among children that match these criteria. This approach requires a multidisciplinary effort to assure the best healthcare support for these patients. Further studies are required to assess what exact pathophysiological mechanisms underlie these observations.

Disclosure: Nothing to disclose

P0382

IBD-RELATED MALIGNANCIES OBSERVED IN 2015-2019 - 4 YEARS' RESULTS FROM THE PROSPECTIVE, NATIONWIDE HUNGARIAN REGISTRY

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Introduction: Patients with inflammatory bowel disease (IBD) have an increased risk to develop malignant neoplasms, particularly colorectal cancer in ulcerative colitis (UC), small bowel cancer in ileal Crohn's disease (CD) as well as cholangiocarcinoma in colitis-associated PSC; however other extra-intestinal malignancies can also occur. Disease-, patients- and therapy related causes are taken into consideration; however, neither the exact mechanism, nor the frequencies of different malignancies are completely clear.

Aims & Methods: Our aim in this prospective, nationwide study was to assess the IBD associated malignancies, to collect clinical and mortality data and to analyse possible risk factors. Data on malignancies developed between January 2015 and May 2019 in Hungarian IBD patients were recorded. Each members of the Hungarian Society of Gastroenterology (HSG) were prospectively interviewed at every 6 months by personal e-mails to report malignancies observed in their patient population. The following data were collected in excel-sheets: demographic data including gender, age at the time of the diagnosis of IBD, disease characteristics of their IBD, such as type and the nature of IBD, previous immunosuppressive or biological therapy, patient adherence, age at the time of the malignancy, and data regarding any malignancies like localization, grade or TNM stage of the tumour and previous colonoscopy report in case of colorectal cancer.

Results: 140 IBD patients with newly diagnosed malignancy were reported by the members of the HSG. The majority of patients were male (female:male ratio was 35:65%; 49:91 patients). 61.4%, 35.7%, and 2.9% of the patients had UC, CD and indeterminate colitis, respectively. The mean age of the patients at the time of initial diagnosis of malignancy was 52.9±14.6 (range 14-92) years; there was no statistical difference in gender. The mean time elapsed between the diagnosis of IBD and the malignancy was 15.1±10.9 (range 0-52) years. According to our results, CRC was the most common cancer (49.6%, 70). 72.9% (51 of 70) of the CRC cases was associated with UC, more than 80% of them had extensive (50.9%, 26) and left-sided (31.2%, 16) colitis. Mean disease duration of IBD with CRC was 17.8±11.5 years, but it was less than 8 years in 10 patients (70% of them had early stage CRC). According to our results, 21.4% of the patients with CRC was non-adherent to regular check-ups. Family history was positive to CRC in 15.7% of the patients. The most common CRC localization in UC patients was the rectosigmoid part of the colon 27 (54.9%), and the rectum in CD patients (7, 38.9%). The most common non-CRC malignancies were non-melanotic skin-cancer (5.7%, 8), haematological and pulmonary cancer (5.7-5.7%, 8-8). Disease duration at the time of the diagnosis

of malignancy was lower (17.8 ± 11.5 vs. 12.6 ± 9.7 years); mean age at the time of the death was higher (49.3 ± 9.4 vs. 64.3 ± 16.4 years); and survive was longer (0.73 ± 1.01 vs 1.2 ± 0.8) after the diagnosis of extraintestinal malignancy compared to CRC.

Conclusion: CRC presented typically in the distal part of the colon by male UC patients with pancolitis or left-sided colitis with a long-standing disease course of IBD. The most common non-CRC malignancies were non-melanotic skin cancer, haematological cancer and lung cancer. Patients with non-CRC malignancies were typically female and older than CRC patients at the time of the diagnosis of malignancy with shorter disease-course of IBD and longer survival.

Disclosure: Nothing to disclose

P0383

SYSTEMATIC REVIEW AND META-ANALYSIS: THE IMPACT OF CONCOMITANT IMMUNE-MEDIATED DISEASES ON THE DISEASE LOCALIZATION AND BEHAVIOUR IN PATIENTS WITH CROHN'S DISEASE

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Introduction: A unique phenotype of ulcerative colitis in association with primary sclerosing cholangitis (PSC) is recognized and well characterized in the literature, but data on the phenotype of Crohn's disease (CD) in presence of PSC and other immune-mediated inflammatory diseases (IMIDs) are inconsistent.

Aims & Methods: The aim of this study was to conduct the first systematic review with meta-analysis investigating the impact of co-occurring IMIDs on disease location, behavior and risk of CD-related surgeries. PubMed and EMBASE were searched from database inception till October 2019 for studies reporting prevalences or odds, risks or hazard ratios of disease localization and behavior of CD according to the Montreal or Vienna Classification in patients with and without co-occurring IMIDs. Meta-analyses were performed using the DerSimonian and Laird random-effect model. Secondly, metaregression was conducted to investigate the risk of CD-related surgery in relation to the disease location and behaviour. The quality of the studies was assessed by the Newcastle-Ottawa Scale (NOS).

Results: The literature search retrieved 4,067 studies of which 23 studies comprising 1,572 CD patients with IMIDs and 35,043 CD patients without IMIDs fulfilled the inclusion criteria. The mean NOS quality score was 7.6 including 21 high quality studies and two studies of moderate quality. Overall, patients with CD and co-occurring IMIDs had no clear pattern of CD disease localization but subgroup-analysis on CD patients with PSC showed that presence of co-occurring PSC was associated with a lower risk of ileal inflammation (L1) (RR=0.44 (95%CI 0.24-0.81), $p < 0.01$, $I^2 = 32\%$) and an increased risk of isolated colonic inflammation (RR=1.78 (95%CI 1.33-2.38), $p < 0.01$, $I^2 = 32\%$).

The presence of IMIDs was in general associated with an increased probability of a non-stricturing and non-penetrating behavior both in presence of PSC (RR=1.43 (95%CI 0.97-2.11), $p = 0.07$, $I^2 = 86\%$) and IMIDs other than PSC (RR=1.33 (95%CI 1.03-1.71), $p = 0.03$, $I^2 = 85\%$). CD patients with co-occurring IMIDs had similar risk of surgery compared to patients without co-occurring IMIDs (RR=1.00 (95% CI 0.91-1.14), $p = 0.96$, $I^2 = 23\%$), but subgroup analysis of patients with co-occurring PSC showed that these patients had a significantly lower risk of CD-related surgeries (RR=0.55 (95%CI 0.34-0.88), $p = 0.01$, $I^2 = 0\%$).

However, metaregression analysis found that this risk was not associated with the localization or behavior of CD. In accordance with previous stud-

ies, we found colonic involvement (L2 and L3) to be associated with CD-related surgery, both among CD patients with and without co-occurring IMIDs ($p < 0.01$).

Conclusion: This first systematic review and meta-analysis found that CD patients with co-existing PSC - similar to ulcerative colitis patients - have a unique inflammatory distribution primarily confined to the colon and a non-stricturing and non-penetrating behavior which is associated with a halving of the relative risk of CD-related surgeries compared to patients without co-occurring PSC. This study emphasizes the importance of recognizing IMIDs among patients with CD and their prognostic role in the disease course of CD.

Disclosure: Nothing to disclose

P0384

ABDOMINAL AORTIC CALCIFICATION AS A MARKER OF CHRONIC INFLAMMATION-MEDIATED ATHEROSCLEROSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Accumulating evidence has associated abdominal aortic calcification (AAC) with risk factors of cardiovascular disease (CVD). Computerized-tomography (CT) and computerized enterography (CTE) are often performed in patients with inflammatory bowel disease (IBD).

Aims & Methods: The aim of the present study was to compare AAC between IBD patients and matched controls and to evaluate a possible association with disease characteristics. This is a retrospective analysis of data derived from 88 (67 with CVD, 21 without CVD) consecutive IBD patients [63 males, 59 Crohn's disease (CD), median age 59 years (range 23-86 years), mean ($\pm$ SD) age at diagnosis 40.8 ± 14.8 years and mean follow-up of 12.8 ± 10.6 years].

The grade of AAC was compared between IBD patients with CVD and 1:1 ratio age and gender matched non IBD patients with CVD and IBD patients without CVD and 1:1 ratio age and gender matched non IBD patients without CVD who had performed abdominal CT or CTE at the outpatient clinic. History of malignancy, rheumatic disease or chronic renal disease were among exclusion criteria for non IBD patients. IBD patients with history of malignancy were also excluded. Parameters expressing disease severity [IBD related surgeries, hospitalizations for flare, IBD medication, disease extent (>40 cm ileal involvement for CD or extensive colitis for ulcerative colitis (UC)), and traditional CVD risk factors [smoking, obesity, hypertension, dyslipidemia and diabetes mellitus] were recorded.

Results: History of treatment with anti-TNF was reported in 55.7%, IBD related surgery in 19.3% of IBD patients. As expected IBD patients with CVD had statistically significant higher rates of moderate-severe AAC compared to IBD patients without CVD (66.7% vs 25.4%, $p = 0.001$). No difference in the degree of AAC was found among all IBD patients and the control group (moderate severe AAC 35.2% vs 28.4%, $p = 0.419$). IBD patients without CVD had higher rates of moderate-severe AAC compared with non IBD patients without CVD (58.6% vs 41.4%, $p = 0.402$). Moderate-severe AAC was found more frequently among UC compared to CD patients (55.2% vs 25.4%, $p = 0.009$), in patients with non use of anti-TNF ($p = 0.007$) and non use of steroids ($p = 0.009$).

No association between IBD related surgeries, mean rate of hospitalizations for flare and immunomodulators' use with the grade of AAC was found. Extensive disease was more frequently associated with milder AAC

grade ($p=0.021$). After multivariate adjustment for classical CVD risk factors only less extended disease ($p=0.012$) remained independently associated with more severe AAC.

Conclusion: Aortic calcification evaluated by CT scans seems to be similar in IBD patients and matched controls and not significantly correlated with disease characteristics. Larger prospective studies are needed.

Disclosure: Nothing to disclose

P0385

PERCEPTION OF THE ROLE OF FOOD AND DIETARY MODIFICATIONS IN THE GENESIS OF SYMPTOMS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND IMPACT ON LIFE STYLE

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Introduction: Inflammatory bowel disease (IBD) are chronic inflammatory intestinal disorders of the gastrointestinal tract of unknown etiology. The increasing incidence and prevalence of IBD among countries adopting a “Western diet”, suggests diet as a factor involved in the pathogenesis of IBD.

In addition, dietary components have been found to influence gastrointestinal symptoms. Many patients change their food habits after the diagnosis in the aim to reduce symptoms and prolong the remission period and some follow restrictive diets that can lead to malnutrition and to a significant reduction in the quality of life.

Aims & Methods: The aim of this study is to evaluate food habits and nutrition knowledge in patients with IBD. A semi-structured questionnaire assessing personal data, weight, height, ethnic group, qualification, tobacco use, medical history, surgical history, IBD type (UC or CD), time of diagnosis, disease activity (remission, mild, moderate or severe), symptoms, treatment, dietary behavior and gluten or/and lactose intolerance, was developed. The questionnaire was administered to 167 consecutive patients with IBD attending our tertiary center for infusion of biologics (84 pts) or for follow-up visits (83 pts).

Results: The majority of patients did not consider food a cause of their disease. However, 82.1% of patients in the biologics group, including 28(73.7%) with UC and 41(89.1%) with CD, and 81.9% of patients in the group treated with conventional therapy, including 36(83.7%) affected by UC and 32(80.0%) with CD, changed their diet after the diagnosis though treating physicians advised there is limited evidence of no correlations between IBD and diet and that a definite IBD diet does not exist.

Age, sex, marital status, smoking habit and type of IBD were not related to dietary changes. Having changed diet, 53.6% of patients treated with biological therapy, and 76.5% of those on conventional therapy, experienced improvements in symptoms, ($p<0.05$) while the rest of the patients found no benefit. Elimination of food was less common in pts on biologics ($p=0.01$) and in females.

A dairy-free diet is followed by 50.0% of patients of the first group, and 33.7% of patients of the second group. The elimination of this type of food is mainly, but not exclusively, linked to the fact that dairy products triggered symptoms of the diseases. Because of the disease, 52.4% of the infusion room patients, and 39.8% of the other group have changed their lifestyle.

Conclusion: Most of the patients set diet and life style on self-experience and give up many foods. This might have an impact on psychosocial functioning, causing a lack of enjoyment and fear of eating and making social occasions stressful. A stronger effort is warranted in providing multidisciplinary

care to IBD patients with the presence of qualified dietitians to fill the gap between patients' concerns about food and existing evidence and wise recommendations of healthcare professionals.

Disclosure: Nothing to disclose

P0386

GENETIC TESTING OF HLA-DQA1-HLA-DRB1 IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Thiopurines remain important therapeutics in the management of Crohn's disease (CD) and ulcerative colitis (UC), but despite their clinical effectiveness, thiopurines present clinicians with several challenges including their narrow therapeutic index and risk of adverse drug reactions (ADR) [Srinivasan A. et al., 2019]. Using of proactive therapeutic drug monitoring in Inflammatory Bowel Disease (IBD) patients can facilitate early treatment decisions and lead to better treatment outcomes [Khan A. et al., 2019]. Sazonovs A. et al. (2018), demonstrated in their study that immunogenicity to anti-TNF is determined by HLA variants. Recent studies on HLA demonstrated a significant link between HLA-DQA1-HLA-DRB1 single-nucleotide polymorphism (SNP) rs2647087 and thiopurine-induced pancreatitis [Wilson A. et al., 2019]. The underlying mechanism of this dose-independent immune-mediated allergic reaction is still unknown [Burnet G. et al., 2019].

Aims & Methods: Our aim was to evaluate HLA-DQA1-HLA-DRB1 polymorphism in IBD patients in Latvia. In our prospective study blood samples were collected from 67 IBD patients (52% women; 48% men) in Genome Database of the Latvia Population. HLA-DQA1-HLA-DRB1 genotyping with real-time qPCR for the detection of rs2647087 was used. Categorical data were analysed by the Pearson's χ^2 test; Fisher exact test was used if the number in any expected cell < 5 (SPSS®23).

Results: Among patients, 58 % ($n=39$) had UC, median age 40.2 years (Q1-Q3=30.0-45.0) and 42% (28) had CD, median age 40.1 years (Q1-Q3=28.5-54.0). 68.4% of UC patients had total UC and 15.8% had left-sided colitis. Mostly 44.7% patients had moderately active UC (Mayo score 6-10), for CD patients median CDAI was 157 (Q1-Q3=125.78-270.0). 34.3% were using thiopurine group medications (mostly AZA) and only 6% were under biologic anti-TNF therapy at that moment. HLA-DQA1-HLA-DRB1 genotype in 38.8% was of the former carrying a wild-type homozygous genotype (A/A), 46.3% carrying heterozygous (A/C) and 14.9% of homozygous genotype (C/C). Those with a homozygous genotype before had an experience of using AZA and had pancreatitis as ADR. In total 7.5% patients described different ADR when using AZA, as myelosuppression, gastrointestinal intolerance.

Conclusion: Our study identified SNP rs2647087 located on HLA-DQA1-HLA-DRB1 polymorphism in adult IBD patients and showed a heterozygous genotype as the most prevalent. 14.9% of patients are at risk of ADR that indicates a high prevalence of HLA polymorphisms. Targeted phenotyping and genotyping gives important information for prediction of thiopurine and thiopurine plus anti-TNF therapy induced ADR.

Disclosure: Nothing to disclose

P0387

CLINICAL OUTCOME AFTER ILEO-RECTAL ANASTOMOSIS VS ILEAL POUCH IN ULCERATIVE COLITIS IN A LONG-TERM FOLLOW UP

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Introduction: In Ulcerative Colitis (UC), surgery is required in about 5-20% of patients (pts). Evidences regarding the long-term outcome of UC patients after ileo-rectal anastomosis (IRA) vs the more recently proposed ileal pouch anastomosis (IPAA) are still lacking.

Aims & Methods: In a real-life, retrospective, single-center study, we aimed to compare, in a cohort of UC pts under regular follow up, the clinical outcome after IRA versus IPAA.

In a retrospective study, clinical records of all UC pts with IPAA or IRA under regular follow-up from January 2001 to September 2019 at our referral IBD Unit were reviewed. Inclusion criteria: 1) Well defined diagnosis of UC; 2) Age ≥18 yrs; 3) IPAA or IRA for UC; 4) Available detailed clinical history; 5) Follow up ≥1 yr after surgery. The following demographic and clinical characteristics were reported in a shared database: hospitalization, additional abdominal-related surgery, mortality, ileal and rectal dysplasia/cancer, number of endoscopies and of outpatient visits after surgery (n/yr), daily stool frequency (median), UC-related treatments (steroids, thiopurine or methotrexate, biologics). The quality of life (QoL) was evaluated in subgroups of patients. Data were expressed as mean [range], differences between groups were assessed by using the chi-squared or unpaired T-tests.

Results: Among a 2136 UC pts in follow up, a total of 84 (4%) pts had a history of IPAA (n=47) or IRA (n=37). Among these 84 UC pts, A detailed clinical history after surgery (≥1 yr follow up), was available in 38 (45%) of pts (22 IPAA, 16 IRA). The mean follow up in these 38 pts was 72 [12-180] months (mos) and the mean time interval from surgery was 72 [1-348] mos. In the 22 pts with IPAA (9 M, 13 F) and in the 16 pts with IRA (6 M, 10 F), the mean age at first assessment was 46 [30-56] and 48 [23-82] (p=0.75), respectively. The mean follow up after surgery was 65 [12-132] mos vs 79 [12-180] (p=0.83).

The mean time interval from surgery to first clinical assessment was 60.1 [1-312] vs 74.28 [2-348] mos (p=0.20). Indication for surgery was refractory UC in 37 pts and endoscopic perforation in 1 pt. During the follow up after surgery, the following major outcomes were significantly more frequent in pts with pouchitis vs IRA: hospitalizations for pouchitis or IRA-related symptoms (pts: 9 vs 0, p=0.032) and mean daily stool frequency (7.5 vs 4.3; p=0.0001).

Additional intestinal surgery was the only clinical outcome more frequent in pts with IRA vs pouchitis (n=2 vs n=6 pts; p=0.034). The following clinical outcome did not differ between pts with pouchitis vs IRA: hospitalization for any intestinal symptom (number of pts: 8 vs 7; p=0.64); UC related mortality (n=0 vs n=1 pts, p=0.23); development of dysplasia/cancer of the ileum or rectum (n=0 vs n=2 pts; p=0.08), number of endoscopies after surgery (mean/yr: 0.78 vs 0.64; p=0.59), number visits after surgery (mean/yr: 2.21 vs 1.84; p=0.81), pts requiring biologics after surgery (n=5 vs n=0; p=0.06).

Conclusion: In a preliminary real-life experience, differences were observed in terms of major clinical outcomes after IRA or IPAA for UC. The stool frequency and the number of UC-related hospitalizations were more frequent in pts with IPAA. Differently, the need of additional abdominal surgery was more frequent in pts with IRA.

Disclosure: Nothing to disclose

P0388

NEW DIAGNOSTIC CAPABILITIES FOR CROHN'S DISEASE: USE OF FATTY ACID PROFILES OF ERYTHROCYTE MEMBRANES AND BLOOD SERUM

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Introduction: The fatty acids, in particular the n-3 and n-6 PUFAs, mediate a number of key biological processes, including production of eicosanoids, inflammation, physiological processes in the cell membrane, gene regulation and expression [1].

Aims & Methods: The purpose of this research is to investigate the features of the fatty acid composition of erythrocyte membranes (Er) and blood serum (BS) among patients with Crohn's Disease (CD) for possible use in differential diagnosis.

We have examined 22 patients with CD, 21 patients with inflammatory bowel diseases unclassified (IBDU) (35.2±4.7 years), and 20 healthy individuals, which are comparable in age and gender to the main groups. The study of the composition of fatty acids (FAs) of Er and BS has been carried out using a gas chromatography-mass spectrometry (GC/MS) system based on the Agilent 7000B Triple Quadrupole (USA).

Results: The levels of most saturated, monounsaturated omega-9 (palmitoleic C16:1n-9, oleic C18:1n-9), omega-6 PUFAs have been significantly higher among patients with Crohn's disease, and the predominant part of omega-3 (including eicosapentaenoic (C20:5 n-3), docosapentaenoic (C22:5 n-3), docosahexaenoic (C22:6 n-3) is lower than among healthy individuals (p<0.001-0.05). The relative content of FAs among patients with inflammatory bowel disease unclassified has happened to be interim in comparison with those for patients with CD and healthy ones.

The content of palmitic (C16:0), digomo-γ-linolenic (C20:3 n-6), arachidonic (C20:4 n-6) acids in the BS and Er membranes of the patients with CD has been significantly higher, and linoleic acid (C18:2 n-6) is lower than among healthy individuals (p<0.001-0.05), which indirectly indicates an increased activity of delta-6-desaturase with a likely violation of the feedback mechanism. An increased level of palmitic and palmitoleic FA in BS and in Er membranes among the patients with CD associated with reduced stearic content (C18:0) reflects a reduced activity of elongase-6. A high content of palmitic acid C16:0 can induce macrophages that actively secrete inflammatory cytokines in the intestinal mucous membrane [2]. The increased metabolism of the linoleic acid with a formation of the arachidonic acid, a precursor of bioactive eicosanoids (prostaglandins, leukotrienes, thromboxanes and lipoxins), is caused by an active inflammation and an increased platelet aggregation, including in the intestinal mucous membrane [3]. Elevated levels of C20:3 n-6 + C20:4 n-6/ C18:2 n-6

and C16:0/ C18:2 n-6 ratios have been found among patients with CD in comparison to them among healthy patients ($p < 0.001$) both in erythrocyte membranes and in serum. When performing a ROC analysis with these indices, high AUC values have been obtained when distinguishing the patients with CD from healthy ones (Er membranes for C16:0/C18:2 n-6-AUC 0.89, sens. 0.82, spec. 0.88); for C20:3n-6/C20:4n-6 / C18:2 n-6-AUC 0.81, sens.0.86, spec.0.74). We established differentiating values of FA levels for patients with CD, with which the FA levels of the patients with IBDU had been compared. Among 8 patients with IBDU, index levels have been within the range of those among patients with CD; among seven patients, Crohn's disease has subsequently been verified, which indicates a high potential of this approach for differential diagnosis.

Conclusion: The revealed features of the FA levels of Er and BS membranes, as well as their ratios among patients with CD, are promising for the purposes of differential diagnosis, including in cases of indeterminate colitis.

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Disclosure: Nothing to disclose

P0389 WITHDRAWN

P0390

SCREENING FOR IRON-DEFICIENCY IN NON-ANEMIC PATIENTS WITH IBD: DOES IT MATTER?

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Introduction: Anemia is the most common extraintestinal complication of inflammatory bowel disease (IBD). Iron-deficiency (ID) may be found in patients with normal hemoglobin (Hb) levels, causes fatigue and impairs quality of life (QoL). ID alone develops prior to anemia, although existing data is scarce regarding its prevalence and management.

Aims & Methods: Aim of the study was to assess and characterize ID in IBD patients.

The present study included 108 patients with IBD and available laboratory data including iron studies (total blood count, serum iron, ferritin, fecal calprotectin). Presence or absence of anemia was assessed based on Hb level: Hb less or more than 12 g/dl (female) or 13 g/dl (male). Presence of ID was assessed based on ECCO criteria: ID was defined as a ferritin < 30 µg/L in the absence of inflammation or ferritin < 100 µg/L in the presence of inflammation. Inflammation was assessed by fecal calprotectin (< 50 mg/kg means no inflammation and >50 mg/kg means inflammation). Demographic data, disease duration and fatigue were recorded from each patient. We excluded 23 patients with anemia from chronic diseases or other types of anemia. The rest of the patients (n = 85) were divided into

three groups: G1 (IDA) = 41 patients (48.2%), G2 (non-anemic ID) = 23 patients (27.1%), G3 (without anemia, without ID) = 21 patients (24.7%). Fatigue was assessed by FACIT-F Scale in each group.

Results: Mean FACIT-F scores in G1, G2 and G3 were 30 ± 6, 32 ± 5, and 43 ± 3 respectively. Statistical significant difference was noted between mean FACIT-F score in G1 vs G3 ($p < 0.05$) and G2 vs G3 ($p < 0.05$). The mean FACIT-F score was not statistically different in G1 vs G2 ($p > 0.05$). Severe fatigue (FACIT-F < 30 points) was reported in 41% of patients in G2 and 39% of patients in G1 ($p > 0.5$). Severe fatigue was not reported in G3 patients. Therapy with iron preparates increased mean FACIT-F scores in G1 and G2: 44±6 in G1 and 43 ± 5 in G2 ($p < 0.05$).

Conclusion: Iron deficiency is present in a high proportion of non-anemic patients with IBD and has the same impact on fatigueness like IDA. Routine assessment of iron status is important to institute early recognition and treatment in order to prevent IDA and its clinical consequences.

Disclosure: Dumitru Eugen and Alexandrescu Luana: speakers for Alfa Sigma Wassermann and Abbvie.

P0391

IGA VASCULITIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASES: A MULTICENTER STUDY OF THE GETAID AND GFEV

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Introduction: IgA vasculitis (IgAV) associated with Inflammatory Bowel Disease (IBD) is rare and poorly known. Few case reports suggested an association of IgAV with anti-TNF therapy in IBD. Our aims were to describe the characteristics and prognosis of IgAV in a retrospective cohort of patients with IBD.

Aims & Methods: Patients with IgAV and IBD were included in a multicenter cohort study conducted by the GETAID and the French vasculitis study group (GFEV) from November 2018 to February 2020. Charts were retrospectively reviewed. IBD was diagnosed according to usual criteria. IgAV diagnosis was considered as definitive (IgA deposits in biopsy) or probable (purpura features, other organ, no differential diagnosis) according to the American College of Rheumatology criteria. Characteristics of IBD (type, extent, phenotype, treatments) and the IgAV (clinical, biology, treatment, evolution) were collected using a standardized anonymous questionnaire. Descriptive statistics were used.

Results: Out of 60 reported cases, 43 were included in 17 centers [21 women, 25 (58%) Crohn's disease (CD) and 18 (42%) ulcerative colitis (UC)]. IBD preceded IgAV in 38 (88%) cases, with median interval of 9.2 (interquartile range (IQR), 5.4-15.4) years. In these patients, CD location was ileal, colonic, ileocolonic, and anoperineal in 5 (17%), 3 (13%), 14 (61%) and 14 (58%) respectively and UC was rectal, left sided or pancolitis in 3 (7%), 6 (29%) and 9 (57%) respectively. Median ages at IBD and IgAV diagnosis were 26 (IQR, 19-33) and 39 (IQR, 26-49) years, respectively. At IgAV diagnosis, 5 patients (13.5%) had active IBD and 29 (78%) were treated

with anti-TNF (adalimumab 52%, infliximab 48%) for a median duration of 31 (IQR, 19-55) months. IgAV diagnosis was definitive in 28 (74%) and probable in 10 (26%). Main clinical features were purpura (100%), joint involvement (53%), gastrointestinal (29%) and renal (47%). IgAV was treated in 35 (78%) patients with steroids (68.5%), colchicine (16.6%), cyclophosphamide (17%) or other (11.5%). Anti-TNF was stopped in 15 (52%) and switched to 5-ASA (n=3), ustekinumab (n=4), vedolizumab (n=3), azathioprine (n=5). No IgAV relapse was observed in patients who stopped anti-TNF vs. 31 % in patients continuing anti-TNF.

After anti-TNF cessation, 35.7% had an IBD flare or a complication vs. 7.7% in patients continuing anti-TNF. Anti-TNF was resumed in 6 (40%) patients [same anti-TNF (n=3), other anti-TNF (n=3)] with subsequent IgAV relapse in 60%. Overall, after a median follow up of 17.3 months (IQR, 6.9-49), 14% of patients had at least 1 IgAV relapse: purpura 86%, joint 36%, renal 14%, gastrointestinal 7%. Evolution of IgAV was favorable except in 4 patients with chronic renal failure including 1 kidney transplant. Two patients died during follow-up (cardiogenic shock during renal transplant, sepsis in a patient with neoplasia).

Conclusion: In a large cohort of IBD patients who developed subsequent IgAV, we found that most patients were treated with anti-TNF agents. IgAV evolution after stopping and resuming anti-TNF therapy suggests a key role of anti-TNF agents in this condition.

Disclosure: Nothing to disclose

P0392

EVALUATION OF ANORECTAL FUNCTION IN PERIANAL CROHN'S DISEASE: A PILOT STUDY

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Introduction: Perianal Crohn's disease (CD) is a disabling condition, with little known about anorectal function in healed/inactive perianal CD.

Aims & Methods: This study aimed to evaluate anorectal function in a homogeneous cohort of patients with treated/healed perianal CD.

This was a prospective cohort study performing high-resolution anorectal manometry with balloon distention, a balloon expulsion test and 3D-endoanal ultrasound (EAUS) in all patients. Patients with a previous vaginal delivery or active proctitis were excluded.

Results: Of the 16 patients studied (mean age $\pm$ SD, 42 $\pm$ 13 yrs), 12 (75%) were men. A laceration of the internal anal sphincter and/or anal scarring was seen in nine (56%) patients; there was no laceration of the external anal sphincter. Five (56%) of these nine patients had never experienced faecal incontinence. All had normal anal resting and squeeze pressures. Manometry suggested dyssynergia in 11 (69%) patients, with only one (6%) fulfilling the criteria for obstructed defecation. Hyposensitivity for at least one sensory parameter (first sensation, desire to defecate and maximum tolerated volume) was seen in 11 (69%) patients and hypersensitivity in five (31%) patients.

Conclusion: This first study to systematically evaluate anorectal function in patients with treated perianal disease detected sphincter abnormalities (by EAUS) in more than half of patients, many of whom were asymptomatic. This might be relevant in asymptomatic women with inactive perianal

CD when selecting the future mode of delivery. Alterations in rectal sensation were frequently seen, more commonly with rectal hyposensitivity.

TRIAL REGISTRATION: ClinicalTrials.gov (NCT03819257)

Disclosure: Nothing to disclose.

P0393

FATIGUE IS ASSOCIATED WITH DISEASE-SPECIFIC BEHAVIOUR IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: A substantial group of patients with inflammatory bowel disease (IBD) experience fatigue, even while in clinical remission¹. At present, disease-specific behaviours that maintain or worsen symptom burden including fatigue have not been explored. We developed a questionnaire evaluating IBD-specific avoidance behaviour and investigated how this relates to self-reported fatigue.

Aims & Methods: This study was a close collaboration between the psychology and gastroenterology department of our tertiary referral center. A 72-item IBD-specific avoidance behaviour questionnaire (IBD-B) was generated based on literature review and input from clinicians and a patient focus group (N=10). Between July 2018 and March 2019, 500 consecutive IBD patients were included at our infusion unit (wave 1) (participation rate 79%, 48% male, 66% Crohn's disease (CD), median age 40). Patients completed the 72-item IBD-B, a demographic questionnaire, patient-reported outcome assessing disease activity (PRO2) and a Visual Analogue Scale (VAS) for fatigue. Clinical remission was defined as an abdominal pain score $\leq$ 1 and a liquid to very soft stool frequency $\leq$ 1.5 in CD patients and as no rectal bleeding and a stool frequency score $\leq$ 1 in patients with ulcerative colitis (UC). Test-retest reliability was assessed in 89 patients (54% male, 70% CD, median age of 40) who completed the IBD-B, PRO2 and VAS fatigue scale a second time after 4-12 weeks (wave 2). A principal component analysis (PCA) was then used to reduce the number of items and investigate the underlying factor structure of the IBD-B. Lastly, we analysed the predictive value of IBD-specific behaviours for fatigue both cross-sectionally and prospectively.

Results: At wave 1, respectively 46% and 69% of CD and UC patients were in clinical remission. PCA suggested a reduction of the 72-item to a final 25-item IBD-B and a seven-factor solution for use in clinical practice (loading factors $>$ 0.5). The final 25 item IBD-B showed good psychometric properties. The median (IQR) total IBD-B and fatigue scores were, respectively, 29 (40-20) and 52 (77-25) for patients in clinical remission compared to 38 (48-28) and 74 (87-50) for patients not in clinical remission (both $p < 0.01$). Cross-sectional and prospective correlations between IBD-B factors and fatigue are demonstrated in the table.

Conclusion: The IBD-B is a reliable tool to assess a range of disease-specific behaviours in IBD patients. IBD patients, even those in clinical remission, show significant correlation between avoidance behaviour and fatigue. Targeting IBD-specific avoidance behaviours may be a promising strategy to prevent fatigue unrelated to inflammation. The next step is to use the IBD-B large scale in clinic to address the prospective correlation between behaviour and fatigue in patients in clinical remission.

	Test-retest	Fatigue (wave 1)	Fatigue (wave 2)	
IBD-B factors and items (wave 1)	N=89	Clinical remission N=246	No clinical remission N=216	All patients N=87
Avoidance of certain food and activities	0.84	0.377**	0.485**	0.438**
Ensuring toilet access	0.89	0.247**	0.240**	0.334**
Reduced sexual activity	0.91	0.138*	0.277**	0.226*
Cognitive avoidance	0.81	0.094	0.064	0.037
Not sharing with others	0.85	0.144*	0.296**	0.179
Alternative treatments	0.85	-0.030	0.16*	0.102
Active disease management	0.63	0.114	0.139*	0.087

*Significant at the 0.05 level (2-tailed); **Significant at the 0.01 level (2-tailed); Patients with missing values (IBD-B score, fatigue score, C-reactive protein or disease activity) were excluded from the correlation analysis.

[PCA results (Cronbach's alpha) and Pearson correlations, controlled for C-reactive protein]

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P0394

FIRST SUCCESSFUL COMPARISON OF QUANTUM BLUE® RAPID TDM ASSAY STANDARDIZATION WITH WHO INTERNATIONAL STANDARD FOR INFLIXIMAB

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Introduction: Therapeutic drug monitoring of IBD patients under anti-TNF therapy is based on trough level determination of the drug. Rapid assays and multiple ELISAs are available that measure anti-TNF biologics. An international standard is required to improve comparability among different assays. Recently, WHO introduced a series of anti-TNF standards for etanercept, adalimumab and infliximab. This is the first step for achieving common standardisation of assays available on the market.

Aims & Methods: The aim of the study was to evaluate the correlation of the WHO standard with BÜHLMANN Quantum Blue® Infliximab standardization and to compare spiking recovery in three commercially available infliximab ELISAs and one infliximab rapid test. Calibration curves were generated with BÜHLMANN calibrators and with calibrators made from WHO international standard for infliximab (NIBSC 16/170). Twenty-six serum samples, covering a concentration range from 0.5 µg/mL to 19 µg/mL,

were analyzed with both calibration curves and compared by Bland-Altman and Passing-Bablok analysis. Furthermore, recovery of six serum samples spiked with WHO international standard for infliximab was determined in Theradiag LISA TRACKER Infliximab (a), Grifols/Progenika Promonitor-IFX (b), Immundiagnostik IDKmonitor Infliximab drug level (c) and BÜHLMANN Quantum Blue® Infliximab (d). Spiking recovery experiments were performed according to Westgard 2008.

Results: The sample values gained with BÜHLMANN calibrators showed an excellent correlation with values gained with the WHO international standard for infliximab as calibrator. Passing-Bablok regression analysis revealed a slope of 0.96 and correlation coefficient (R) of 0.99. Bland-Altman analysis revealed a mean difference in the obtained values of less than five percent. Regarding spiking recovery analysis, all tests exhibit an excellent mean recovery of 101% (85-114%; a), 99% (91-105%; b); 101% (95-107%; c) and 94% (88-100%; d).

Conclusion: Current standardization of Quantum Blue® Infliximab rapid test correlates very well with the WHO international standard for infliximab (NIBSC 16/170). Spiking recovery was highly comparable for ELISAs and the Quantum Blue® Infliximab assay. This rapid test represents a unique and modern analytical method, for fast time-to-result and simplicity of usage in a more patient near medical environment.

Disclosure: Nothing to disclose

P0395

LOW ADHESION TO LATENT TUBERCULOSIS (TB) SCREENING RECOMMENDATIONS IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS: RESULTS OF THE INFEII REGISTRY OF GETECCU

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Introduction: INFEII registry (ClinicalTrials.gov: NCT02904590) is a prospective study promoted by GETECCU to determine the incidence and risk factors of infection in an inception cohort of IBD patients. Despite preventive measures and recommendations of scientific societies, TB remains a problem in patients with IBD treated with immunosuppressants (IMM) and biologics.

Aims & Methods: **Aims:** To assess: 1) the screening of TB performed at the time of inclusion of a patient in the INFEII registry, 2) the incidence of latent TB; and 3) compliance with national and European recommendations.

Methods: A longitudinal prospective study of incident cases with IBD, initiated in October 2016 and with a planned follow-up of 5 years. In September 2019 INFEII registry had 1239 patients from 28 centres throughout Spain. The study protocol determines the mandatory fulfilment of TB screening in every patient, leaving to the centre the freedom of decision on what procedures to perform. Guidelines recommend a mandatory study before starting immunosuppression, especially with biological treatment, using the combination of tuberculin skin test (TST) and interferon-gamma release assay (IGRA) or at least one TST with a booster test (Riestra, EII al dia, 2015; Rahier, JCC, 2014).

Results: Of the 1239 patients 130 (10%) had no screening, 391(32%) had one [TST 132, IGRA 225, thorax-X-ray 34], 412 (33%) two [TST + IGRA 92, IGRA + thorax-X-ray 230, TST + thorax-X-ray 56, TST + booster 34], 181 (15%) three [TST + IGRA + thorax-X-ray 114, TST + booster + IGRA 14, TST + booster + thorax-X-ray 53] and 125 (10%) the four tests [TST + booster + IGRA + thorax-X-ray]. 485 patients (39%) receive pharmacological immunosuppression (172 IMMS, 193 biologics, 120 COMBO) and from them 227 (47%) followed the guidelines recommendation (100 TST-IGRA, 56 TST-booster and 71 TST-booster-IGRA), 248 (51%) had some method for TB screening [TST 24, IGRA 60, thorax-X-ray 10, IGRA + thorax-X-ray 119, TST + thorax-X-ray 35] and 10 patients (2%) had no screening. With the baseline screening, latent TB was detected in 147 patients (12%), 72 (49%) receiving anti-TB chemotherapy. In patients initiating immunosuppression, latent TB was detected in 38 cases [of which 30 received prophylaxis but 8 under IMM did not]. Active TB was detected in 4 cases: 2 during baseline screening, one without screening and one with negative screening (negative TST and IGRA, without booster receiving biological treatment).

Conclusion: Despite TB in IBD is a relevant problem, there is ample room for improvement for the implementation of mandatory minimum screening recommendations, even in prospective protocolized projects.

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P0396

CHARACTERISTICS OF ULCERATIVE COLITIS PATIENTS BY URGENCY OF DEFECATION AT ENROLLMENT IN THE CORRONA INFLAMMATORY BOWEL DISEASE REGISTRY

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Introduction: There is little real-world data describing characteristics of Ulcerative Colitis (UC) patients according to urgency severity, or whether those characteristics differ for patients on biologics or Janus kinase inhibitors (JAKi) vs conventional therapy.

Aims & Methods: Describe UC patients on biologic/JAKi or conventional therapy by urgency severity and assess the association of urgency severity with patient-reported outcome measures.

UC patients in the Corrona IBD Registry between 5/3/17-1/2/2020 (n=875) were included in the study. Patient-reported/physician-recorded urgency was assessed within the Simple Clinical Colitis Activity Index (SCCAI) as urgency of defecation by none (N), hurry (H), immediately (IM), and incontinence (IN).

Patient characteristics were compared by urgency level H vs N, IM/IN combined vs N based on effect sizes, i.e., standardized differences >0.10. Descriptive analyses were repeated after stratifying by patients on biologic/JAKi therapy (n=224) or conventional therapy (n=322). Associations of higher urgency (N, H, IM/IN) with number of prior biologic/JAKi medications, disease severity, symptoms, Patient-Reported Outcomes Measurement Information System (PROMIS) scores (categorized as: < 55, within normal limits; 55-60, mild; and >60, moderate/severe), and Work Productivity Activity Impairment (WPAI) indices were assessed using Spearman or Kendall correlations and trend tests (Jonckheere-Terpstra or Cochran Armitage).

Results: Among 832 UC patients with no proctocolectomy, 87.3% were in remission/mild disease, and 488 had N, 265 had H, 62 had IM, and 17 had IN urgency. Most demographics, comorbidities, and disease characteristics did not significantly differ across urgency levels. Compared to N, patients with H or IM urgency were slightly more likely to be female, current smokers, have Medicaid insurance, "other" work status, and a lower mean duration of current IBD therapy. Notably, 29.7% and 48.4% of H patients and 17.2% and 46.6% of IM patients were in remission or had mild disease, respectively.

Higher (worse) urgency was correlated with a higher number of prior biologics/JAKi (p< 0.05), worse disease severity (partial Mayo Score, 0-9), symptoms (day and night bowel frequency, number and frequency of daily stools, blood in stool/rectal bleeding), patient and physician-reported global assessment, higher number of extra-colonic features, and higher (worse) PROMIS scores and WPAI indices (p=0.001 for all). Compared with N, patients with IM/IN urgency were more likely to have moderate/severe PROMIS scores for fatigue (13.5% vs 44.7%), sleep disturbance (6.2% vs 24.4%), pain interference (9.4% vs 40%), depression (4.9% vs 21.8%), and anxiety (13.9% vs 33.8%).

Of note, compared to N, even H urgency was associated with almost twice the prevalence of moderate/severe scores for fatigue, sleep disturbance, pain interference, depression, and anxiety. Similarly, for WPAI indices, mean %s were higher for patients with H and IM than N urgency (p=0.001 for all): absenteeism (15% and 7% vs 4%), presenteeism (43.5% and 23.6%

vs 10.2%), work productivity loss (45.6% and 26.3% vs 11.3%) and activity impairment (48.9% and 30.1% vs 11.6%), respectively. Similar trends were seen for patients on conventional or biologic/JAKi therapy.

Conclusion: Urgency is a common, distinct symptom of UC, and can occur even in remission. Among UC patients in a real-world setting, urgency was associated with a negative impact on sleep, mood, fatigue, and general function. There is a substantial unmet need to identify and improve this symptom.

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P0397

RISK OF PROGRESSION OF PRECLINICAL ULCERATIVE COLITIS

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Introduction: The diagnosis of Ulcerative Colitis (UC) is usually established after the development of symptoms, but preclinical disease may be present months to years before the final diagnosis. During follow-up, around 25% of UC patients can show a proximal extension of the disease.

Aims & Methods: The primary aim of the study was to define the main characteristics and the risk of progression of preclinical UC. We performed a multicentric, retrospective study of all patients included in the colorectal cancer screening programme in 11 centres between 2009-2014. All subjects were initially assessed with a faecal occult blood test (FIT; OC-Sensor, Eiken Chemical Co., Tokyo, Japan) and, if this test was positive (cut-off 20 µg Hgb/g), a colonoscopy was performed. All patients where asymptomatic and had an incidental diagnosis of UC confirmed by histology during a screening colonoscopy. The main outcomes were the risk of developing symptomatic disease and proximal disease extension. A chi-square test was performed in order to assess the risk factors of proximal extension and symptomatic disease.

Results: During this period we performed 31,005 colonoscopies after 498,227 FIT. We included 79 patients with a new diagnosis of UC (age 58 years [IQR, 52-63], 37% non-smokers). At baseline, disease extension was

E1 in 32%, E2 in 33% and E3 in 35%. After a median follow-up of 29 months (IQR, 17–41), 76% received at least one treatment, and no patient showed proximal disease extension. In 45% (33% E3 and 12% E2) we observed a reduction of the disease extension. Among those subjects who were asymptomatic at diagnosis, 32% developed symptomatic disease after a median of 7.5 months (IQR, 1–14). Disease extent at diagnosis did not influence the risk of symptomatic disease during follow-up ($p=0.85$). Those patients with left-sided or extensive UC were more frequently treated with mesalazine, systemic steroids or thiopurines, compared to those with proctitis ($p=0.001$, 0.023 and 0.047, respectively).

Conclusion: Approximately one third of patients with preclinical UC develop symptomatic disease, but we observed no risk of proximal disease extension after 2 years of follow-up. Some cases may show a reduction of the disease extension after starting treatment.

Disclosure: Nothing to disclose

P0398

WEEK 6 CALPROTECTIN BEST PREDICTS LIKELIHOOD OF LONG-TERM ENDOSCOPIC HEALING IN CROHN'S DISEASE: A POST-HOC ANALYSIS OF THE UNITI/IM-UNITI TRIALS

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Introduction: There is need for biomarkers as predictors of outcome to medical treatment in Crohn's disease. The purpose of this study was to evaluate the predictive performance of fecal calprotectin for short- and long-term clinical and endoscopic outcomes.

Aims & Methods: This *post-hoc* analysis of the UNITI/IM-UNITI studies (NCT01369329, NCT01369342, and NCT01369355; YODA #2019-4026) included 677 patients to evaluate the relationship of week 6 calprotectin cut-offs and changes from baseline assessments in calprotectin for prediction of clinical outcomes at week 8, 32, and 52, and endoscopic outcomes at week 8 and 52 using receiver operating characteristic curves with comparisons of areas under the curve (AUC). The relationship between clinical and biomarker assessments at week 6 and endoscopic remission (ER) at week 52 was evaluated using multivariate logistic regression models adjusted for confounders.

Results: A week 6 calprotectin < 250 mg/kg demonstrated a significant ability to predict week 52 ER (AUC 0.709, 95% CI 0.566–0.852, $p=0.014$) with fair accuracy, and performed better than other calprotectin cut-offs and deltas from baseline for prediction of week 52 ER. When adjusted for co-variables, patients with a week 6 fecal calprotectin < 250 mg/kg had 3.48 times (95% CI 1.31–9.28, $p=0.013$) increased odds of week 52 endoscopic remission compared to patients with higher fecal calprotectin levels. No other week 6 clinical assessment (clinical remission or clinical response) or biomarker (CRP < 5 or drug level) had an association on its own with week 52 ER.

Conclusion: In summary, the results of this *post-hoc* analysis suggest week 6 calprotectin levels < 250 mg/kg can be predictive of future endoscopic healing and may be more informative than clinical response or remission. These findings question whether clinical symptom assessments should be relied upon for deciding treatment response and re-randomization in clinical trials.

Disclosure: Nothing to disclose

P0399

REAL WORLD USE OF THE IBD DISK TOOL IN UNSELECTED COHORTS OF OUTPATIENTS

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Introduction: The IBD Disability Index (IBD-DI) is a validated health care professional (HCP) administered tool that can assess the functional status of patients in trials. The IBD-Disk was adapted from the IBD-DI as a tool that patients can use to capture their functional status for HCPs to review. We report patient acceptability and use of the IBD-disk in the real world setting.

Aims & Methods: The IBD-Disk was constructed by an expert steering committee of international gastroenterologists/nurses who ranked the IBD-DI items. A modified Delphi process was used to agree on 10 IBD-Disk items. It was administered in outpatient clinics to patients across NHS hospitals. Inclusion criteria comprised patients aged 18 and over, of all ethnicities, with a confirmed diagnosis of IBD. Exclusion criteria were lack of fluency in English, not agreeable to take part or participation was deemed inappropriate. Patients were asked to rate their level of agreement for each item on the IBD Disk on a visual analogue scale of 0–10 (0 = absolutely NO, 10 = definitely YES). We included a difficulty rating of 1–10 to assess ease of completion of the questionnaire (1=very easy; 10=very difficult) as well as qualitative feedback.

Results: A total of 377 patients agreed to take part. The mean age of the cohort was 42 years. 221 were female (59%). 287 were White. 199 patients had CD, 159 UC, the remaining unknown. Of the domains of the IBD Disk, energy levels, sleep and joint pain scored highest (most impairing) with mean values of 5.68, 4.85 and 4.68 respectively whereas interpersonal interactions and sexual functions were least affected, mean scores 2.51 and 2.81. The mean difficulty rating was 2.3 (SD=2.29). Correlations were performed between abdominal pain and energy levels/ sleep ($r=0.6$ and $r=0.56$) and between joint pain and energy levels/ sleep ($r=0.57$ and $r=0.58$). Clinicians highlighted that the IBD-disk opened up conversations beyond GI issues and gave a good overview of wellbeing. It facilitated discussion on sexual function and body image. Patients' feedback highlighted that they were glad they were able to express their functional status and its severity.

Conclusion: Energy levels, sleep and joint pain were the most disabling for this unselected IBD cohort. This may help to focus the discussion in the clinic setting. Our experience with the IBD-Disk proved very positive with high patient acceptability.

Disclosure: Nothing to disclose

P0400

IMPACT OF ABDOMINOPELVIC RADIOTHERAPY ON INFLAMMATORY BOWEL DISEASE ACTIVITY: A MULTICENTER COHORT STUDY FROM THE GETAID

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Introduction: Abdomino-pelvic radiotherapy in Inflammatory Bowel Disease (IBD) patients raises concerns regarding the risk of worsening the underlying disease. Our study aimed at comparing incidence rate of IBD activity before and after abdomino-pelvic radiotherapy as well as flare-free survival rates and factors associated with flare after radiotherapy in IBD patients.

Aims & Methods: From 1999 to 2019 a retrospective multicenter study including consecutive IBD patients exposed to at least one abdomino-pelvic irradiation treatment was conducted, collecting data on IBD activity by semesters before (from S-4 to S-1) and after (from S+1 to S+6) radiotherapy and, on IBD flare - defined as clinical symptoms associated with introduction or intensification of any systemic drug, and/or an hospitalization and/or a digestive or perianal surgery - during follow-up.

Results: Sixty-one patients (32 women, mean age 59 years, 25 UC and 36 CD), corresponding to 467 semesters, treated for digestive (n=31), urinary tract (n=23) and gynecological cancers (n=7) were included in 18 centers. Incidence rates of IBD activity per semester were respectively 0.21 (CI95%-0.16-0.27) from S-4 to S-1, 0.12 (CI95% 0.07-0.19) from S+1 to S+3 (p=0.15 vs S-4 to S-1) and 0.16 (CI95% 0.10-0.25) from S+4 to S+6 (p=0.45 vs S-4 to S-1). With a median follow up of 36 (19-84) months, 8 (13%) patients died and 1 patient underwent abdominal surgery.

Rates of survival without IBD flare at 1 and 3 years after radiotherapy were 82.5% (CI95% 73.2-93.0) and 70.6% (CI95% 58.8-84.7), respectively. Mod-

erate-to-severe acute gut toxicity of radiotherapy (OR=6.34; CI95% 1.82-22.08) and urinary tract cancer (OR=6.13; CI95% 1.26-29.72) were independently associated with an increased risk of IBD flare during follow-up.

Conclusion: The majority of patients with preexisting IBD can be safely treated by abdomino-pelvic radiotherapy. Considering the association between acute gut toxicity and increased risk of IBD flare, lowering as much as possible the dose to the gut tissue should be recommended to the radiation oncologists. Patients with urinary tract cancer or having a moderate-to-severe acute toxicity should be more closely monitored in the post-radiotherapy period.

Disclosure: Nothing to disclose

P0401

EVALUATION OF INTEREST AND KEY FEATURES OF A HEALTH CARE APP TO ASSIST IN THE MANAGEMENT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE AMONGST CLINICAL TRIAL SITES IN THE UNITED STATES

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Introduction: The use of mobile apps to support management of IBD patients is increasing. One addition to the use of these apps could be pre-screening of patients for IBD clinical trials.

Aims & Methods: Evaluate [1] interest of inflammatory bowel disease (IBD) investigators in a mobile phone health care app for patients with Ulcerative Colitis (UC) or Crohn's Disease (CD) to support patient management and pre-screening for clinical trials [2] key features of an IBD app which would assist patient management or identification of patients for clinical trials.

IQVIA conducted an online survey among IBD investigators in the United States between February and March 2020. A five-point Likert scale from "Not at all useful" to "Extremely useful" was used to evaluate the usefulness of app features.

Results: A total of 61 investigators from academic medical centers, private practice, and dedicated research centers responded to the survey. 8% (5/60) currently ask their patients with UC or CD to use a health care app to track symptoms and detect flares.

When asked if they would be willing to use IQVIA Flare Check to supplement IBD patient care in their practice and potentially identify patients with UC or CD who may be suitable for a clinical trial, 69% (42/61) responded "yes" or "unsure". The following results are based on the 41 individuals within this group who provided responses.

To help them manage patients with UC or CD, 98% (40/41) indicated that alerts when flares are detected, utilising pre-specified clinical criteria built into the app, would be moderately to extremely useful; followed by graphs of historical symptoms in weekly, monthly, and quarterly views at 93% (38/41); and real-time visibility into patients' symptoms of rectal bleeding, stool frequency and abdominal pain, via an online portal at 88% (36/41).

To help them enroll clinical trials, 98% (40/41) reported that assessing real time symptom diaries would be moderately to extremely useful, followed by engaging patients in clinical trials; and reducing screen failure through better visibility into patient symptoms at 90% (37/41).

From the patient perspective, 93% (38/41) reported that flare detection and communication of symptoms and flares with their doctor in real time would be moderately to extremely useful, followed by the ability to look for trends in symptom history through simple graphs at 90% (37/41) and the increased opportunity to participate in clinical trials at 83% (34/41).

63% (26/41) have >20 patients within their practices for whom they would IQVIA prescribe Flare Check.

Conclusion: Only 8% of investigators are currently asking their patients to use a healthcare app to track symptoms and detect flares, yet more than half would be willing to use an app featuring flare alerts, real-time visibility into patient symptoms, and graphs of historic symptoms.

In conclusion, there is a significant unmet need for technology that [1] connects patients with their physicians to improve patient management, as well as [2] enroll clinical trials with the opportunity to assess compliance with symptom diaries and reduce screen failure through visibility into patient symptoms.

Disclosure: Nothing to disclose

P0402

SERUM CALPROTECTIN IS NOT EFFECTIVE TO PREDICT IBD RELAPSE AND HAS WEAK DIAGNOSIS ACCURACY

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Introduction: Serum calprotectin (SC), a novel biomarker of inflammatory bowel diseases (IBD), has been recently investigated with some conflicting results. The purpose of this study was to assess the ability of SC for predicting disease relapse in patients with IBD treated by biologic therapies, and to evaluate the correlation of SC with clinical disease activity, mucosal healing and with other biomarkers (FC and CRP).

Aims & Methods: 119 consecutive IBD patients in deep remission were recruited in this prospective study from the IBD Unit of Saint Etienne in France. SC was measured and correlated with clinical activity and mucosal healing at each visit. We evaluated the role of SC to predict relapse in IBD, compared with C reactive protein (CRP) and fecal calprotectin (FC), its diagnostic performance and its correlation with fecal calprotectin.

Results: During follow-up, 46.4% (n=54) relapsed. In these patients, we found no elevation of SC before relapse with medians at 3.15, 3.38, 3.33, 3.99 µg/l, at time 0, 120, 240 and the day of relapse, without significant difference between these medians (p=0.63).

A low correlation was found between SC and FC levels with a Pearson coefficient at r=0.35, (P= 0.001).

When all the assays (489) were evaluated to compare patient with deep remission or not, SC and FC in patients with mucosal healing are significantly lower than that in patients without mucosal healing (3.57 µg/ml (IQR 2.38-5.31 µg/ml) and 29.8 µg/mg (IQR 16.0 - 99.0 µg/mg) versus 4.79 µg/ml (IQR 3.58- 7.66 µg/ml) and 352.7 µg/mg (IQR 136.0 - 1472.0 µg/mg; p=0.02 and < 0.002 respectively), but with an important overlap of confidence interval for SC.

Moreover, the sensitivity and specificity of SC (cutoff level, 3.68 µg/ml) for diagnosing mucosal healing was 53% and 73.8% with an area under the curve of 0.63, compared to 0.86 and 0.74 for FC and CRP respectively. The diagnostic performance was a little better for UC compared to Crohn's disease.

Conclusion: SC failed to predict relapse, while we actually found an elevation of FC before relapse. The performance diagnostic of SC was low with an AUC of 0.63, lower than CRP and FC.

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Disclosure: pfizer, abbvie, amgen

P0403

PRIMARY STUDY RESULTS FROM GO OBSERVE: A REAL-WORLD EUROPEAN PROSPECTIVE SINGLE-ARM OBSERVATIONAL COHORT STUDY OF PATIENT-REPORTED CONTINUOUS CLINICAL RESPONSE TO GOLIMUMAB IN ADULTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

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Introduction: The use of frequent (q4wk) office visits to assess maintenance of clinical response in patients with ulcerative colitis (UC) using the Mayo score,¹ as was done with golimumab (GLM) in the PURSUIT studies,^{2,3} is not practical in clinical practice. The combined score for the patient-reported stool frequency and rectal bleeding components of the Mayo score (known as PRO2) has been shown to be an accurate measure for monitoring maintenance of treatment response in UC.⁴⁻⁶ The GO OBSERVE study examined whether the results of the PURSUIT studies translate into clinical practice in the European Union (EU) and assessed whether patient-reported continuous clinical response (pCCR; based on PRO2 reporting q4wk) is an effective real-world outcome measure for monitoring the maintenance of GLM-induced clinical response.

Aims & Methods: GO OBSERVE was a multicenter, prospective, single-arm, exploratory, observational cohort study conducted at 43 outpatient clinics across 8 EU countries. The study enrolled 109 adult patients with moderately to severely active UC (Mayo score ≥6 and endoscopic sub-score ≥2) who were biologic-naïve or had been exposed to at most one other biological therapy. Patients received induction with SC GLM 200 mg and 100 mg at Weeks 0 and 2, respectively, followed by maintenance with SC GLM 50 mg (if body weight < 80 kg) or 100 mg (if body weight ≥80 kg or if inadequate response to 50 mg at Week 6) every 4 weeks, starting at Week 6 and continuing to Week 54. Clinical response was assessed at the end of induction (Week 6, 10, or 14, depending on local practice) based on full or partial Mayo score (see footnote 'a' in table). During maintenance, patients self-reported their stool frequency and rectal bleeding scores q4wk using an electronic data capture system, which was accessed by investigators to monitor PRO2 score throughout the study. The analysis population for the primary and key secondary efficacy endpoints included all patients who completed induction in clinical response and who had received full GLM induction treatment (responders). The primary efficacy endpoint was the proportion of responders in pCCR through Week 54 of GLM maintenance based on PRO2 q4wk and partial Mayo score at Week 54 (see footnote 'b' in table). The proportion of responders in remission at Week 54 was a key secondary endpoint (see footnote 'c' in table).

Results: For the 109 enrolled patients, 52 (47.7%) were female, mean age was 38.9 yrs, and 83 (76.1%) were biologic-naïve. Thirty-seven of the 109 patients (34.0%) were responders (table); 30 (81.1%) of the 37 responders were biologic-naïve. At Week 54, among the 37 responders, 15 (40.5%) were in pCCR, 21 (56.8%) were in remission, and 4 (10.8%) were in corticosteroid-free remission (table).

Entered induction phase (safety population), N	109
Completed induction phase, n/N (%)	89/109 (81.7)
___Completed induction in clinical response ^a and received full golimumab induction treatment (responders), n/N (%)	37/109 (34.0%)
Primary Endpoint: Responders in pCCR ^b at Week 54, n/N (%)	15/37 (40.5)
Key Secondary Endpoint: Responders in remission ^c at Week 54, n/N (%)	21/37 (56.8)
___Responders in corticosteroid-free remission at Week 54, n/N (%)	4/37 (10.8)

^aClinical response to induction treatment was defined as a decrease from baseline in the partial Mayo score $\geq 30\%$ and ≥ 3 points with either a decrease from baseline in the rectal bleeding sub-score ≥ 1 or a rectal bleeding sub-score of 0 or 1, or it was defined as a decrease from baseline in the full Mayo score $\geq 30\%$ and ≥ 3 points with an endoscopic sub-score of ≤ 2 and either a decrease from baseline in the rectal bleeding sub-score ≥ 1 or a rectal bleeding sub-score of 0 or 1.

^bpCCR=patient-reported continuous clinical response, defined as continuous absence of clinical UC flare during maintenance, based on PRO2 reporting q4wk and partial Mayo score at Week 54. UC flare was defined as an increase of PRO2 with ≥ 2 points at any of the 4-weekly symptom reporting times and followed by UC treatment change, UC-related hospitalization or surgery as decided by the investigator or their designee. Patients who were lost to follow-up or who prematurely discontinued the study and did not reach the Week 54 primary endpoint were considered non-pCCR (treatment failures).

^cRemission was defined as absence of active UC symptoms as assessed by a PRO2 score ≤ 1 or a (partial) Mayo score of ≤ 2 with no individual subscore > 1 .

[Table]

Conclusion: Regular remote monitoring of PRO2 appears to be a meaningful real-world outcome measure for monitoring the maintenance of GLM-induced clinical response. The results of this study confirm the effectiveness of GLM in the induction and maintenance of clinical response in patients with moderately to severely active UC over 54 weeks in a real-world setting.

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P0404

METHOD COMPARISON STUDY OF TWO COMMERCIALLY AVAILABLE TDM TEST FOR THE MEASUREMENT OF USTEKINUMAB LEVELS

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Introduction: Therapeutic Drug Monitoring (TDM) of Ustekinumab (UTK) may be useful to complement clinical assessment and optimize patients' treatment. Various commercial IVD tests to monitor UTK levels in serum are available. Here we present a method comparison study between two commercially available CE-marked tests.

Aims & Methods: A prospective, observational cohort study was conducted in the IBD outpatient Clinic at the University Hospital Erlangen (Germany) in patients with Crohn's disease (CD) treated with UTK. Trough UTK and anti-UTK antibody levels were measured with Promonitor®-UTK and Promonitor® Anti-UTK tests (Progenika, Spain), respectively, and compared to the corresponding results using LISA TRACKER Ustekinumab (LTU) (Theradiag, France) in 100 serum clinical samples collected at baseline and during the course of treatment. Both tests are based on ELISA technology to quantify UTK and anti-UTK antibodies levels. The limit of quantification of the tests is 0.06 µg/mL and 0.04 µg/mL for Promonitor®-UTK and LTU, respectively. The study was performed following the Package Insert instructions provided by each manufacturer. All statistical analysis performed used a non-parametric approach (JMP software 14.0).

Results: Here we report results for 30 patients (100% CD) recruited so far. UTK was administered every 8 weeks. Measurement of drug levels was performed in all patients after induction and during maintenance therapy. Using the standard sample dilution recommended in the LTU insert (1:101), the test resulted in a low number of samples (58, 58%) within the limit of detection of the test, which obliged to perform a reflex testing with a higher sample dilution with the consequent loss of time and reagents. Seventy five and 23 samples were positive and negative for UTK levels, respectively, in both Promonitor-UTK and LTU.

The remaining two samples were negative for Promonitor-UTK and positive for LTU. The quantitative comparison of the two tests was done only with the results obtained for both assays (n=75). Median UTK levels was 2.62 µg/mL (0.19-15.23) and 2.92 µg/mL (0.21-17.67) for Promonitor-UTK and LTU, respectively. The Pearson Correlation value was 0.956 and the average difference was 13.6% between Promonitor-UTK and LTU. Passing-Bablok regression analysis showed that UTK levels results correlated but the confidence interval of the intercept and slope did not include zero (-0.26 to -0.05) and slope and one (1.17 to 1.34), respectively, showing a systematic proportional slightly difference between the two tests.

The variability is proportional to concentration which can be expressed as a constant CV. Whereas agreement was good below 3 µg/mL of UTK, Bland-Altman analysis showed a systematic slightly difference between both measurements above 3 µg/mL.

None of the patients in the cohort developed antibodies against UTK.

Conclusion: UTK levels are in line with those reported in other studies in IBD. Both assays correlate and can be used for monitoring of UTK levels, however the measurement range and the sample dilution recommended by Promonitor-UTK covers more accurately the UTK concentrations found in CD's patients, whereas use of the LTU forces the user to repeat the testing or perform two sample dilutions by default because the recommended sample dilution is not appropriate for the population. In the absence of a gold standard method to unequivocally assess tests accuracy, UTK

concentration results measured with different tests should be taken with caution and it is advised that monitoring drug concentrations in patients over time would be best done using a single test.

Disclosure: Torres N, Apraiz I., Landeta M., Nagore D. and Lopez M. are a full time employees of Progenika. Atreya R. and Neurath M. received honoraria for lectures and consulting fees from Janssen-Cilag

P0405

THE VARIABILITY IN THE DISTRIBUTION OF HISTOLOGICAL ACTIVITY IN COLONIC SEGMENTS IN PATIENTS WITH ULCERATIVE COLITIS AND THE IMPACT HEREOF ON THE DEVELOPMENT OF AI TOOLS

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Introduction: Currently, new artificial intelligence tools are being developed that assess histological activity in ulcerative colitis (UC). These tools evaluate focal areas of inflammation in one colonic segment. However, data on the distribution of the histological inflammation within one segment are lacking. This impacts on the reliability of the histological activity scores and on the results of real-time virtual histological assessment by new endoscopic techniques.

Aims & Methods: The aim of this study was to assess the variability in histological activity within one endoscopic segment in patients with UC. Sequential patients with UC and planned endoscopy were included. Standard and virtual endoscopic biopsies were taken in 3 contiguous areas of 12 mm diameter (central/ adjacent above/ adjacent below) within the visually normal appearing or continuous inflamed colonic segment (rectum/sigmoid/descending). Biopsies were scored for the Geboes score (GS), Robarts histological index (RHI) and Nancy histological index (NHI). Cut-offs for histological non-remission were GS $\geq$ 2B.1, RHI $>$ 3 and $>$ 6, NI $\geq$ 2. Kappa statistics (Cohen and Fleiss) for categorical outcomes and intraclass correlation coefficient (ICC) for continuous outcomes were used to assess variability.

Results: A total of 161 biopsy sets originating from 55 endoscopic segments of 21 patients were available for analysis. Endoscopic active disease (Mayo endoscopic subscore $>$ 0) was present in 54% of the segments. The continuous histological scores showed excellent agreement between the different regions in one segment. The ICC for RHI in all segments was 0.926 (95% confidence interval (CI): 0.885-0.954) and 0.942 (95% CI: 0.910-0.965) for the numerically converted GS. Results were comparable between the different segments. The categorical NHI, in contrast, showed higher variability with a $\kappa=0.574$ for all segments and $\kappa=0.473$, 0.636 and 0.621 for rectum; sigmoid and descending colon respectively. In all segments the highest variability was seen in samples with NHI=2 or 3. When dichotomizing the scores in histologic remission versus non-remission a good agreement was seen for all score: GS $\geq$ 2B.1 $\kappa=0.734$ (95%CI: 0.729-0.740), RHI $>$ 3 $\kappa=0.79$ (95%CI: 0.785-0.795), RHI $>$ 6 $\kappa=0.895$ (95%CI: 0.890-0.900), NI $\geq$ 2 $\kappa=0.734$ (95%CI: 0.729-0.740) in all segments. The homogeneity in the distribution of the histological disease activity was comparable between the different colonic segments.

Conclusion: Distribution of histological disease activity in UC follows a homogeneous pattern in different locations of one segment. Therefore, in an endoscopic continuous inflamed or normal colonic segment, the location of biopsies in adjacent parts of one colonic segment does not impact on the histological disease activity score.

Fleiss kappa	all segments	rectum	sigmoid	descending
Geboes remission (cut-off $\geq$ 2B.1)	0.734	0.721	0.712	0.738
Robarts remission (cut-off $>$ 3)	0.79	0.867	0.708	0.738
Robarts remission (cut-off $>$ 6)	0.895	0.936	0.778	1
Nancy remission (cut-off $\geq$ 2)	0.734	0.721	0.712	0.738
Nancy ordinal	0.574	0.473	0.636	0.621

Intraclass correlation coefficient	all segments	rectum	sigmoid	descending
Geboes numeric	0.942	0.943	0.943	0.96
Robarts numeric	0.926	0.902	0.936	0.95

[Variability of histological activity between different locations in one colonic segment]

Disclosure: PB has received financial support for research from AbbVie, Mundipharma, Pfizer, Janssen and Mylan; lecture fees from AbbVie, Takeda, Pfizer and Janssen; advisory board fees from AbbVie, Takeda, Hospira, Janssen, MSD, Mundipharma, Roche, Pfizer, Sandoz and Pentax. RB has received research grant consultancy and speaker's fees: Pentax Medical and Fujifilm SV has received financial support for research: MSD, AbbVie, Takeda, Pfizer, J&J; Lecture fee(s): MSD, AbbVie, Takeda, Ferring, Centocor, Hospira, Pfizer, J&J, Genentech/Roche; Consultancy: MSD, AbbVie, Takeda, Ferring, Centocor, Hospira, Pfizer, J&J, Genentech/Roche, Celgene, Mundipharma, Celltrion, SecondGenome, Prometheus, Shire, Prodiges, Gilead, Galapagos, MRM Health GDH 's institution KU Leuven received fees for his activities as central pathology reviewer in clinical trials of Centocor and Takeda

P0406

INTEGRATION OF EHEALTH FOR PAEDIATRIC IBD IN REAL LIFE IS SAFE

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Introduction: We have shown in a randomized clinical trial that patient-managed eHealth (RCT-eHealth) monitoring of children and adolescents with Inflammatory Bowel Disease (IBD) was feasible with no risk of increased disease activity (www.young.constant-care.com, Carlsen 2016). Since 2016 the same eHealth solution was integrated as a clinical treatment option in standard care (I-eHealth).

Aims & Methods: This study aims to evaluate the risk and benefits of I-eHealth after 3 years follow up. The I-eHealth solution young.constant-care was offered to IBD patients aged 10 to 17 years old given non-biological treatment. The patients used the I-eHealth application monthly and in case of flare-ups. Blood and fecal calprotectin were tested every 3 months and at flareups. Based on symptom score (Paediatric Ulcerative Colitis Activity Index/abbreviated Paediatric Crohn's Disease Activity Index) and level of faecal calprotectin a total inflammation score was calculated and visualized for the patient in a traffic light curve (green: none to mild activity; yellow: moderate activity; red: severe activity). Patients were only seen at one annual preplanned outpatient visit. On-demand outpatient visits were carried out scheduled depending on the total inflammation score (red colour and repeated yellow colour). "Web-rounds" were performed by an eHealth educated nurse. Data were collected from the patient's medical records concerning demographic data, number of contacts

to the hospital, escalation in medication (as a proxy for disease activity) and reasons for ending I-eHealth. Frequencies and survival analyses of time to first escalation in medicine and time to first out-patient visit was compared to results from the RCT-eHealth. In the RCTeHealth, the eHealth group was monitored similarly to the I-eHealth group whereas the control group followed standard monitoring i.e. 4 pre-planned outpatient visits/year.

Results: 36 IBD patients were followed by I-eHealth, 24 ulcerative colitis/12 Crohn's disease, median age 15 (IQR 14-16). The median (IQR) duration of using I-eHealth was 1.9 years (0.29-2.51) equal to 66.11 patient years. Patient years in the RCT-eHealth were 40.45 in the eHealth group and 46.49 in the control group. The number of on demand visit pr. patient year was 1.15, 1.16 and 0.84 pr. patient year in the I-eHealth group/RCT eHealth group/the RCT control group (notice that the control group had 4 pre-planned visits/year compared to 1/year in the eHealth groups). Hospitalizations and acute outpatient visits (discharged same day) were: 0.11 and 0.11, 0.05 and 0.02, 0.11 and 0.11 pr. patient year in the I-eHealth group/RCT eHealth group/the RCT control group, respectively. Comparison of survival analyses of time to first escalation in medicine and time to first on demand visit did not differ between the I-eHealth group and data from the clinical trial (Log rank $p=0.25$ and $p=0.61$, respectively). In total 14/36 patients left the I-eHealth monitoring: 5 patients turned 18 years (transfer to adult departments), 3 patients shifted to biological medication and 4 patients were referred to local hospitals. Only 1 patient wished to stop the I-eHealth monitoring and 1 patient was excluded due to lack of compliance.

Conclusion: I-eHealth for children and adolescents with IBD is safe and matches the results from a RCT.

Disclosure: Nothing to disclose

P0407

A MACHINE LEARNING APPROACH IDENTIFIES SPECIFIC MICROBIOTA SIGNATURE ASSOCIATED TO VARIOUS DEGREE OF ULCERATIVE COLITIS

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Introduction: Ulcerative Colitis (UC) is a complex, immune-mediated disease in which gut microbiota plays a central role. Recent investigations based on 16S rRNA gene sequencing showed significant differences between the microbiota of patients with IBD and healthy controls, suggesting a potential role of gut microbiota in determining worse outcome and disease progression.

Aims & Methods: In this study we aimed to assess whether a specific microbiota profile as measured by a machine learning approach can be associated to disease severity in UC patients.

In this prospective controlled study, consecutive UC patients were enrolled. Stool samples were collected for faecal microbiota assessment analysis by 16S rRNA gene sequencing approach. The microbiota profiles of 36 healthy controls (HCs) were used for comparative analysis. A study of computer algorithms that improve automatically through experience (the machine learning approach) was used to predict the groups' separation.

Results: Forty-six UC patients were enrolled, 20 of them showing mod-

erate-to-severe activity (Active, aUC) and 26 with mild or absent clinical activity (Inactive, iUC). Demographic and clinical features were recorded, including age, sex, localization of the disease, therapy, faecal calprotectin, partial and total and endoscopic-Mayo score Alpha diversity results (OTU richness and Shannon index) showed a marked difference between the three groups. In particular, aUC patients showed the lowest values for both the indices, followed by iUC patients and HC. The detected differences were statistically significant for all the pairwise comparisons, both for richness (p -values: aUC-HC = 0.0009; aUC-iUC = 0.0508; HC-iUC = 0.0079) and for Shannon index (p -values: aUC-HC = 0.0005; aUC-iUC = 0.0273; HC-iUC = 0.0260). *Tenericutes*, *Verrucomicrobia*, *Euryarchaeota* (Archaea) and *Cyanobacteria* were found to characterise HC group, while *Actinobacteria* phylum was significantly more abundant in aUC and iUC patients and a high level of *Proteobacteria* was detected in a consistent subset of aUC patients. At *genus* level, we observed an increase of *Bifidobacterium* and *Haemophilus* in aUC and iUC samples, mainly due to corresponding high proportions of *Bifidobacterium adolescentis* and *Haemophilus parainfluenzae* at *species* level. The application of sPLS-DA, a machine learning supervised approach, allowed us to observe a perfect class prediction and group separation using the complete information (full OTU table), with a minimal loss in performance when using only 5% of features. Interestingly, the great majority of the features selected by the sPLS-DA algorithm were the ones marked as differentially abundant between groups. The host trait predictive potential of the microbiota was also confirmed by a Random Forest analysis.

Conclusion: Implementing current 16S rRNA data with a complex machine learning approach, we were able to identify a bacterial signature characterizing the different degree of disease activity in UC. Follow-up studies will clarify whether such microbiota profiling will predict also disease outcome.

Disclosure: Nothing to disclose

P0408

STRUCTURAL AND FUNCTIONAL CHANGES IN THE BLOOD VESSEL WALL IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Systemic chronic inflammation, specifically attributed to patients with Ulcerative Colitis (UC), is associated with an increased risk of vascular events, however, the direct relationship of cardiovascular events with UC has not been determined. Malabsorption syndrome, chronic blood loss, prolonged inflammatory process affect the structural and functional state of the blood vessel wall.

Aims & Methods: To evaluate structural and functional changes in the blood vessel wall and a number of biomarkers of systemic vascular inflammation in patients with UC.

The study involved 76 patients with UC (men-40.8%, 44.1±4.3 years old) in remission and 40 patients with irritable bowel syndrome (IBS) (men-42.5%, 46.3±5.2 years old). Most of the patients with UC had a moderate severity of the disease (76.3%), severe course was observed in 14.5% of the patients of the group. Patients with UC and IBS did not range in incidence of dyslipidemia (19.7% and 15%), arterial hypertension (28.9% and 25%), and smoking (34.2% and 30%). Explored pulse wave velocity (PWV). Brachial blood pressure was measured non-invasively over 24h with an electronic, oscillometric, automated device (BPLab) with the assessment of 24h central arterial pressure (CAP), reflected wave transit time (RWTT), aortic augmen-

tation index (Aix), arterial stiffness index (ASI). Serum levels of endothelin-1 (ET-1), homocysteine (H), levels of intercellular cell adhesion molecule (ICAM), vascular cell adhesion molecule (VCAM) were measured by ELISA method. Carotid intima-media thickness (CIMT) was evaluated.

Results: An increase level of HZ($17.99 \pm 3.95 \mu\text{mol/l}$), ET-1($4.47 \pm 3.49 \text{ ng/ml}$), adhesion molecules (ICAM-1 363.27 ± 110 , 44 ng/ml and VCAM-1 $986.67 \pm 111.09 \text{ ng/ml}$) were registered in patients with UC compared to patients with IBS ($p < 0.01$). An increase in the average daily values of arterial stiffness monitoring was registered in the group of patients with UC compared to the group of patients with IBS. A significant decrease of RWTT ($118.12 \pm 10.16 \text{ ms}$ and $126.24 \pm 7.98 \text{ ms}$, $p < 0.01$), an increase of PWV ($10.88 \pm 1.78 \text{ m/s}$ and $8.4 \pm 1.4 \text{ m/s}$, $p < 0.001$) was registered in UC patients compared to IBS patients. A significant increase of Aix up to $-5.45 \pm 15.31 \text{ mm Hg}$ was detected in patients with UC and compared to patients with IBS ($-11.94 \pm 17.86 \text{ mm Hg}$, $p < 0.05$), ASI indicators: $139.0 [126.5; 167.0] \text{ mm Hg}$ and $124.0 [117.0; 135.0] \text{ mm Hg}$ ($p < 0.05$). PWV in patients with UC correlated to cardiovascular risk factors: age ($r = 0.53$), SBP ($r = 0.58$), smoking intensity ($r = 0.60$), as well as the frequency of recrudescence over the past 3 years ($r = 0.58$), duration of UC course ($r = 0.56$).

Conclusion: A significant pathological change in the parameters of 24 hour arterial stiffness was registered in patients with UC, regardless of arterial hypertension. In order to identify patients with UC subject to high cardiovascular risk, we recommended testing their arterial stiffness and evaluating functions of endothelium.

Disclosure: Nothing to disclose

P0409

MANAGEMENT AND UNMET NEED AMONGST MILD AND MODERATE/ SEVERE CD AND UC PATIENTS: FINDINGS FROM A CROSS SECTIONAL STUDY IN THE US AND FRANCE, GERMANY, ITALY, SPAIN, UK (EU5)

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases (IBD) that require life-long management. Despite best efforts with newly introduced and existing therapies over the last 20 years, many patients across IBD severity levels still have uncontrolled disease.

Aims & Methods: This study described treatment patterns and clinical status of mild and moderate/ severe patients with CD and UC. This was a cross-sectional study of gastroenterologists and their CD and UC patients in the US and EU5. Data collected from two waves (Nov 2014 - Mar 2015, Sep 2017 - Jan 2018) were merged. Physicians completed patient record forms for their next 8 CD and 7 UC patients, covering disease management, treatment history, clinical outcomes. Same patients completed forms, covering self-reported outcome measures. Data were analyzed based on physician reported current severity assessment of mild and moderate/ severe patients for CD and UC separately. Comparisons between the severity groups were made using Chi Squared, Mann-Whitney and Kruskal Wallis for continuous and categorical variables.

Results: Data from 6150 CD patients and 5331 UC patients were collected. Overall demographic characteristics were similar in the CD and UC cohorts (mean years, age: CD 40, UC 41, time since diagnosis: CD 5, UC 5), including physician-reported disease severity (% mild CD 60, UC 60, % moderate CD 35, UC 35, % severe CD 5, UC 5).

Use of corticosteroids, immunomodulators and biologics was higher

amongst moderate/ severe patients vs mild across CD and UC. The greatest non-remission and flare rates were observed amongst the moderate/ severe populations for both CD and UC. Despite this, disease activity remains high in a considerable subset of mild CD and UC patients: 67% and 60% respectively remain symptomatic and 35% and 39% have flared in the last 12 months.

Comparable levels of concern with the use of steroids and biologics was observed across all severities amongst CD and UC patients with over 25% of all biologic users and over 35% of all steroid users concerned with their treatment use (Table).

	CD Mild	CD Moderate/ Severe	P value	UC Mild	UC Moderate/ Severe	P value
Current treatment class, n	3695	2455		3212	2119	
5-ASA, n (%)	1496 (40.5)	867 (35.3)	<0.01	2116 (65.9)	1232 (58.1)	<0.01
Corticosteroid, n (%)	524 (14.2)	775 (31.6)	<0.01	414 (12.9)	789 (37.2)	<0.01
Immunomodulator, n (%)	1177 (31.9)	935 (38.1)	<0.01	934 (29.1)	708 (33.4)	<0.01
Biologic, n (%)	1329 (36.0)	1152 (46.9)	<0.01	923 (28.7)	745 (35.2)	<0.01
Remission and symptomatic status, n	3695	2455		3212	2119	
Not in remission, n (%)	866 (23.4)	1762 (71.8)	<0.01	683 (21.3)	1627 (76.8)	<0.01
Symptomatic, n (%)	2460 (66.6)	2275 (92.7)	<0.01	1910 (59.5)	1978 (93.4)	<0.01
Known flare status, n	3316	2131		2953	1772	
Flared past 12 months	1175 (35.4)	1394 (65.4)	<0.01	1162 (39.4)	1123 (63.4)	<0.01
Patient concerns (1=not at all, 5=very; 4+5 shown)	179	244		134	270	
Patients on corticosteroids						
Concern with corticosteroid use, n (%)	67 (37.4)	115 (47.1)	0.06	61 (45.5)	118 (43.7)	0.45
Patients on biologics	473	398		313	276	
Concern with biologics use, n (%)	130 (27.5)	135 (33.9)	<0.01	82 (26.2)	93 (33.7)	<0.01

[Table: Mild vs moderate/severe CD and UC: physician reported current treatment and clinical outcomes and patient reported treatment concern level]

Conclusion: Unmet need exist in all severity cohorts across CD and UC. Whilst moderate/ severe patients experience the greatest clinical burden, flares and symptoms also persist amongst substantial cohorts of mild patients, suggesting non optimal disease management. Patients across all severity groups express concerns around their treatment, particularly those on steroids. There is room for improved interventions.

Disclosure: Mirko V. Sikirica is an employee and shareholder of Johnson & Johnson. John Lynch is an employee of Janssen Research & Development. Ben Hoskin, Jim Kershaw, Rosie Wild, and Rina Lukanova are employees of Adelphi Real World.

P0410

INTRODUCTION OF BOWEL ULTRASONOGRAPHY FOR FOLLOW-UP OF PEDIATRIC INFLAMMATORY BOWEL DISEASE: A SINGLE-CENTER EXPERIENCE

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Introduction: Bowel ultrasonography (BUS) for imaging of inflammatory bowel disease (IBD) is increasingly recognized as a prominent noninvasive tool to supplement, and in some cases replace traditional endoscopic and imaging modalities, with high sensitivity and specificity. The increasing number of gastroenterologists trained to perform BUS has transformed BUS into a bedside tool to guide routine clinical decision making and accurately monitor response to treatment. However, this process is still in its infancy in pediatric IBD. We present here data on the first 2 years of implementation of BUS performed by a pediatric gastroenterologist (RLT) at the pediatric IBD center at Shaare Zedek Medical Center in Jerusalem. We aim to describe trends, results and clinical implications of the US studies performed during this period.

Aims & Methods: The electronic medical record system was searched for all BUS studies performed on IBD patients by RLT as part of his weekly IBD clinic between 2017-2019. Studies performed on other caregivers' patients were excluded to ensure uniform documentation and nomenclature. Findings were classified as normal (wall thickness < 3 mm), mild (wall thickening 3-4 mm and blood flow < Limberg 3) or significant signs of inflammation (wall thickness ≥4 mm or 3-4 mm with Limberg ≥3). Charts were reviewed to assess impact of BUS findings on clinical management.

Results: A total of 83 bedside BUS studies were performed on 55 IBD patients (42 with Crohn's - CD) during the study period, with mean age of 15.1±3.7 years. 34 had one study (23 with CD), 15 had two (13 with CD) and 6 had three or more (all with CD). Overall, 32 studies were normal, 20 showed mild findings and 30 showed significant inflammation. Four studies found stenosis and one showed an abscess. Follow-up studies of initially active disease showed 10/16 (63%) with improvement, including 9/16 (56%) with sonographic remission. 22/83 (27%) studies were felt upon review to have had a direct impact on clinical decision-making. These included decisions not to switch therapy due to normal BUS despite symptoms, admission due to discovery of an abscess, decision to escalate therapy due to lack of sonographic improvement, and decision to continue adalimumab in the presence of a stricture due to favorable prognostic characteristics as per the CREOLE study.

Conclusion: Bedside BUS is a practical and useful tool that can be integrated into a pediatric IBD clinic, with the ability to provide relevant information in real time and thus impact on day-to-day patient management.

Disclosure: Nothing to disclose

P0411

PREDICTION OF INFLAMMATORY BOWEL DISEASE COURSE BASED ON FAECAL VOLATILE ORGANIC COMPOUNDS

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Introduction: Faecal volatile organic compounds are gaseous molecules thought to reflect human metabolism and interaction with gut microbiota.

Aims & Methods: In this pilot study, the potential of faecal volatile organic compounds (VOC) analysis for the prediction of inflammatory bowel disease (IBD) course was evaluated.

Patients with established IBD diagnosis were included in two tertiary hospitals. Patients collected two faecal samples with a 3 months interval in the year following inclusion, on which faecal calprotectin and VOC analysis were performed. Biochemically, active disease was defined as faecal calprotectin (FCP) ≥250 mg/g and biochemical remission as FCP < 100 mg/g. Clinically active disease was defined as Harvey Bradshaw Index (HBI) for Crohn's disease (CD) or Simple Clinical Colitis Activity Index (SCCAI) for ulcerative colitis (UC) of ≥5. Clinical remission was defined as HBI < 4 for CD or SCCAI < 3 for UC. From patients meeting the clinical or biochemical disease state criteria on 2 subsequent time-points, the faecal sample collected at this first time-point was included for VOC analysis using gas chromatography - ion mobility spectrometry (GC-IMS) aiming to predict disease state at second time-point.

Results: Total of 182 IBD samples were included in this study. Based on clinical activity scores, 40 samples were remission-remission, 12 remission-exacerbation, 30 active-active, 14 active-remission. Based on FCP, 41 samples were remission-remission, 8 remission-exacerbation, 30 active-active, 7 active-remission. Biochemically, significant differences were found between patients in remission going into exacerbation versus remaining in remission (AUC (95%CI) 0.75 (0.58 - 0.93), and between patients in exacerbation going into remission versus remaining active (AUC (95%CI) 0.86 (0.73 - 0.99). There were no significant differences for these comparisons based on clinical disease activity indices.

Conclusion: Our study outcomes imply that faecal VOC analysis may hold potential as biomarker to predict the IBD disease course. This may add to timely treatment adjustment and prevention of over and under treatment in the future.

Disclosure: S Bosch has nothing to declare. D Wintjens has nothing to declare. A Wicaksono has nothing to declare. M Pierik has served as a speaker for MSD and has received research Grants from European Union and Dr. Falk. J A Covington has nothing to declare. TGJ de Meij has served as a speaker for Mead Johnson. He has received a (unrestricted) research grant from Danone and is member of the advisory board of Winlove BV. NKH de Boer has served as a speaker for AbbVie and MSD and has served as consultant and principal investigator for TEVA Pharma BV and Takeda. He has received a (unrestricted) research grant from Dr. Falk, TEVA Pharma BV, MLDS and Takeda.

P0412

HUMANISTIC BURDEN AND IMPACT OF THE DISEASE IN MODERATE TO SEVERE PATIENTS WITH CROHN'S DISEASE (CD) AND ULCERATIVE COLITIS (UC): FINDINGS FROM A CROSS SECTIONAL STUDY IN THE US AND FRANCE, GERMANY, ITALY, SPAIN, UK (EU5)

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases that require life-long disease management. Patients with UC might be undertreated because of the perception that disease burden is lower than that of CD.

Aims & Methods: This study assessed and compared the level of disease burden in patients with CD and UC based on healthcare resource utilization, health related quality of life (HRQoL) and work productivity in real world practice. This was a cross-sectional study of gastroenterologists and their CD and UC patients in the US and EU5. Data collected from two waves (Nov 2014 - Mar 2015, Sep 2017 - Jan 2018) were merged. Physicians completed patient record forms for their next 8 CD and 7 UC patients, covering disease management, treatment history, clinical outcomes. Same patients completed forms, covering self-reported outcome measures. Data were analyzed based on moderate/ severe patients by disease; comparisons between CD and UC groups were made using Chi Squared, Mann-Whitney and Kruskal Wallis for continuous and categorical variables.

	CD	UC	P value
Clinical status, n	2455	2119	
Not in remission, n (%)	1762 (71.8)	1627 (76.8)	<0.001
Symptomatic patients, n (%)	2275 (92.7)	1978 (93.4)	0.384
Patients with comorbidities, n (%)	1198 (48.8)	971 (45.8)	0.047
Patient reported level of (scale: 0 = no, 10 = extreme)**			
n, Pain, mean	543, 4.1	517, 4.1	0.591
n, Sleep disturbance, mean	543, 3.3	517, 3.4	0.315
n, Fatigue, mean	537, 4.1	516, 3.7	0.003
n, Sexual dysfunction, mean	524, 2.3	497, 2.0	0.048
Hospitalisations and surgery, n	2283	1943	
Hospitalisations past 12 months, n (%)	360 (15.8)	190 (9.8)	<0.001
Hospitalisations for surgery past 12 months, n (%)	45 (2.0)	5 (0.3)	<0.001
n, WPAI, Overall work impairment, %	453, 35.6	385, 41.0	0.008
n, WPAI, Absenteeism, %	491, 13.3	418, 19.0	<0.001
n, WPAI, Presenteeism, %	494, 32.4	420, 35.3	0.116
n, EQ-5D score, mean	931, 0.81	833, 0.80	0.130
n, SIBDQ score, mean	909, 44.0	803, 44.0	1.000
n, SIBDQ Systemic domain score, mean	933, 44.7	828, 45.8	0.081
n, SIBDQ Social domain score, mean	921, 46.2	816, 45.5	0.318
n, SIBDQ Bowel domain score, mean	932, 43.4	824, 42.8	0.291
n, SIBDQ Emotional domain score, mean	931, 42.9	824, 43.2	0.669

[Table 1: Moderate/ severe CD and UC patient outcomes*]

*Sample base sizes vary due to patient self-completion variability

**Data Sep 2017-Jan 2018 wave only

Results: Data on 2455 (2154 moderate, 301 severe) CD patients and 2119 (1880 moderate, 239 severe) UC patients were collected. Patient mean age was 39 years (CD and UC) with 49% (CD) and 44% (UC) female. On average, patients were diagnosed for 4.9 (CD) and 3.5 (UC) years. CD patients more

often received biologic (CD 47% vs. UC 35%) and immunomodulator (CD 38% vs. UC 33%), whilst 5-ASA (CD 35%, UC 58%) and corticosteroid use (CD 32%, UC 37%) was greater in UC.

Symptomatic and comorbidity status, levels of pain, sleep disturbance and sexual dysfunction as well as HRQoL, measured by EQ-5D and SIBDQ, were comparable between CD and UC patients. CD patients were more frequently hospitalized (incl. surgery) and reported greater levels of fatigue. Overall work impairment, driven by absenteeism, and non-remission rates were greater amongst UC patients (Table 1).

Conclusion: Moderate/severe CD and UC patients present with comparable disease burden and HRQoL, whilst UC patients report significantly greater impact on work productivity, perhaps reflective of differing symptom manifestation between CD and UC patients. These findings challenge the perception that disease burden is lesser amongst UC patients, particularly in terms of patient reported impact.

Disclosure: Mirko V. Sikirica is an employee and shareholder of Johnson & Johnson. John Lynch is an employee of Janssen Research & Development. Ben Hoskin, Jim Kershaw, Rosie Wild, and Rina Lukanova are employees of Adelphi Real World.

P0413

QUALITY OF LIFE, FECAL CALPROTECTIN AND ENDOSCOPIC DISEASE ACTIVITY: A STUDY OF CORRELATION IN INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel diseases (IBD), namely Crohn's Disease (CD) and Ulcerative Colitis (UC), are chronic disorders with great impact in patients' quality of life (QOL). The association between clinical, endoscopic and laboratorial findings in CD is inconsistent throughout the literature. Fecal calprotectin (FC) is a widely used laboratory marker that correlates with disease activity. There are QOL questionnaires, validated for IBD patients, providing insight on the patient's daily impairment.

Aims & Methods: **Aim:** To assess the correlation between QOL queries, FC and endoscopic activity, in inflammatory bowel disease patients with colonic involvement versus isolated ileal involvement.

Methods: Retrospective, single center, cohort study. Patients answered a validated QOL questionnaires, namely, the IBD Disability Index (IBD-DI), the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), the Hospital Anxiety and Depression Scale (HADS) and the Patient's Health Questionnaire (PHQ-9). IBD features, patients' demographic and data, laboratorial values and endoscopic findings were collected retrospectively from the medical records. Laboratory findings were collected within an interval of 30 days before or after the questionnaire, and endoscopic findings within 6 months. Univariate analysis tested the association between FC and endoscopic activity. Multiple bivariate logistic regression models tested the homogeneity of the population regarding endoscopic activity. The correlation between FC values and queries scores was tested in linear regression models, splitting the analysis in colonic IBD and isolated ileal disease. ROC curve models tested the accuracy of FC, queries scores and both together, towards the outcome endoscopic activity.

Results: We included 100 patients, 65 CD and 35 UC. Fifty six percent were female and mean age was 38 years old. FC was significantly associated

with endoscopic activity (odds ratio 1.01; $p < 0.001$), this association remained after adjusting to covariables, namely, IBD localization, ileal (DC) or colonic (DC and UC). SIBDQ and IBD-DS were only correlated with FC in colonic IBD (SIBDQ: correlation coefficient -8.853, $p = 0.024$; IBD-DS: correlation coefficient 7.765, $p = 0.021$). The ROC curve model towards endoscopic activity, including only FC displays an area under curve (AUC) of 0.874, $p < 0.001$. The ROC curve model towards endoscopic activity, including FC and SIBDQ displays an AUC of 0.891, $p < 0.001$.

Conclusion: FC is associated with endoscopic activity in both isolated ileal and colonic disease. The correlation between FC and QOL queries was only significant in patients with colonic IBD. SIBDQ together with FC optimizes the prediction model for endoscopic activity versus FC alone, in colonic IBD.

Disclosure: Nothing to disclose

P0414

INFLAMMATORY BOWEL DISEASE AND CONCOMITANT ENDOMETRIOSIS: FREQUENCY AND CHARACTERISTICS IN A MULTIDISCIPLINARY APPROACH

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Introduction: Inflammatory bowel disease (IBD) and endometriosis are both immuno-mediated chronic inflammatory diseases, affecting the young population. IBD and endometriosis share some of the observed symptoms (i.e. abdominal pain). Endometriosis may be associated with other immuno-mediated diseases but its possible association with IBD is undefined.

Aims & Methods: In a multidisciplinary prospective single-center study we aimed to assess the frequency of previously undiagnosed endometriosis in IBD patients referring symptoms compatible with this condition (dysmenorrhea, dyschezia and/or dyspareunia). Secondary end point was to characterize clinical characteristics of IBD and endometriosis in patients with both conditions. In a prospective study, all female IBD patients in childbearing age referring symptoms compatible with endometriosis during a routine gastroenterological follow up visit were enrolled. According to symptoms, gynecological evaluation and transvaginal ultrasonography by a dedicated gynecologist were performed in compliant patients, to search for pelvic endometriosis. Inclusion criteria: 1) female gender; 2) age ≥ 18 and ≤ 50 years; 3) well-defined diagnosis of IBD; 4) symptoms compatible with endometriosis; 5) consent to perform gynecological assessments. Exclusion criteria were: 1) pregnancy; 2) menopause. Characteristics of IBD, endometriosis and adenomyosis were reported according to standard classifications. Data were expressed as median (range).

Results: During the study period, a total of 17 patients were enrolled. Clinical characteristics recorded included: age 40 (35-47) years, body mass index 21.3 (18-25.6), IBD duration 11.2 (1-21) years. IBD cohort included 10 (58.8%) Crohn's Disease (CD) and 7 (41.2%) Ulcerative Colitis (UC) patients. In CD, lesions involved the ileum in 3 (30%), colon in 2 (20%), ileum-colon in 5 (50%). CD behavior was non-stricturing non-penetrating in 7 (70%), stricturing in 2 (20%), penetrating in 1 (10%) patient. History of perianal disease was reported in 4 (40%) patients; surgery for CD in 4 (40%). UC extent included proctitis in 2 (28.6%), left-sided in 4 (57.1%), pancolitis in 1 (14.3%) patient. Dysmenorrhea was reported by 14 (82.3%) patients, dyschezia in 11 (64.7%), dyspareunia in 9 (52.9%). At transvaginal ultra-

sonography, endometriosis in any form was observed in 10 (58.8%) IBD patients, adenomyosis in 9 (52.9%). Both diseases were detected in 8 patients (47%). Deep infiltrating endometriosis was visualized in all the 10 IBD patients, and 7 out of these 10 (70%) patients showed rectal endometriosis. Among the 10 patients with endometriosis, 7 (70%) had CD, 3 (30%) UC. Dysmenorrhea was referred by 7 (70%) IBD patients, dyschezia by 5 (50%) and dyspareunia by 5 (50%) patients. In these 10 patients, concomitant adenomyosis was detected in 6 (60%) patients.

Conclusion: In a pilot study, endometriosis was newly diagnosed in more than half of IBD patients referring compatible symptoms, all showing deep infiltrating endometriosis. A high rate of rectal endometriosis was observed. In IBD patients, particularly in those referring abdominal pain mimicking IBD, additional symptoms compatible with endometriosis should be searched for proper diagnosis, in order to rule out concomitant endometriosis and/or adenomyosis deserving specific treatments.

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Disclosure: Nothing to disclose

P0415

COMPARISON STUDY BETWEEN PROMONITOR QUICK IFX AND QUANTUM BLUE® INFLIXIMAB FOR THE QUANTIFICATION OF INFLIXIMAB LEVELS

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Introduction: Therapeutic Drug Monitoring (TDM) of infliximab (IFX) is a well-established clinical practice to manage patients treated with IFX. The most common tests for TDM are Enzyme-Linked Immunoassays (ELISA). However, ELISA tests require sending out samples to a centralised laboratory and typically results are reported in a few days. During the last two years, rapid tests based on Lateral Flow (LF) technology have been developed as an alternative to ELISA for TDM. LF tests report results in less than 20-30 min and allow clinicians to make management decisions much faster. Promonitor Quick IFX (PQ-IFX) is the only true Point of Care (POC) test for quantifying infliximab in both whole blood (venous and finger prick) and serum samples. The aim of this study was to compare the performance of PQ-IFX to Quantum Blue Infliximab (QB-IFX), a LF rapid test for serum samples only, and to confirm that results can be compared to the reference ELISA test.

Aims & Methods: Two different LF, Promonitor Quick IFX (PQ-IFX) (Grifols) and Quantum Blue® Infliximab (QB-IFX) (Bühlmann) were evaluated. Testing was performed at the department of Cell and Chemical Biology (Leiden University Medical Center) according to each manufacturer's instructions for processing each test in each reader (PQreader and Quantum Blue reader for PQ-IFX and QB-IFX, respectively). Detailed analysis was

performed at Pogenika Biopharma. All samples were provided by Progenika Biopharma. Imprecision (Coefficient of Variation (CV%)) and accuracy (recovery percentage relative to nominal concentrations) was determined testing six different sera spiked with known IFX concentrations (0, 1, 3, 5, 7, 10 and 15 µg/mL) during two consecutive testing days, in five replicates per sample per testing day. To evaluate the performance of both tests, 37 blinded clinical serum samples, previously characterised with Promonitor-IFX ELISA kit (PR-IFX) (Grifols), were analysed. Data analysis was done using a non-parametric approach (JMP v14.0).

Results: PQ-IFX and QB-IFX imprecision values were 14% (9-27) and 17% (6-36) in the whole concentration range, respectively. For those samples with high IFX levels, imprecision values for PQ-IFX and QB-IFX were 11% and 16% respectively at 10 µg/mL; and 27% and 36% respectively at 15 µg/mL.

PQ-IFX and QB-IFX showed an accuracy of 92% (71-108) and 81% (66-90) across the whole concentration range, respectively. At high IFX levels both PQ-IFX and QB-IFX accuracy was 90% and 70% respectively at 10 µg/mL; and 85% and 81% at 15 µg/mL, respectively.

Although, both PQ-IFX and QB-IFX showed a good correlation with ELISA (0.98 and 0.96 correlation coefficients for PQ-IFX vs PR-IFX and QB-IFX vs PR-IFX, respectively), the difference between PQ-IFX and PR-IFX was lower than between QB-IFX and PR-IFX (30% and 46% slope respectively).

Conclusion: The study indicated that PQ-IFX POC test is more precise and accurate than QB-IFX LF rapid test i.e. at IFX concentrations ≥ 10 µg/mL.

The PQ IFX POC test showed a good correlation with Promonitor-IFX ELISA, representing a valuable tool for the clinician to measure IFX levels at the POC.

Disclosure: Ainhoa Ruiz del Agua, Noelia Rapún, M Begoña Ruiz-Argüello, Daniel Nagore and Amagoia Ametzazurra are full time employees of Progenika Biopharma SA, a subsidiary of Grifols SA

P0416 WITHDRAWN

P0417

VACCINES AND IMMUNIZATION STATUS IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE. EVALUATION AT DIAGNOSIS

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Introduction: Paediatric inflammatory bowel disease (PIBD) patients are especially prone to vaccine-preventable diseases and opportunistic infections.

Aims & Methods: The aim was to evaluate the immunization and vaccination status in PIBD. We performed a descriptive and retrospective study that analyzes the immunization and/or vaccination for measles, mumps and rubella (MMR), hepatitis B virus (HBV), chickenpox, cytomegalovirus (CMV) and Epstein-Barr virus (EBV) of PIBD patients in a tertiary paediatric hospital (Jan 2015- Oct 2019) in the first 6 months after diagnosis.

Results: Amongst 57 patients, 17 (30%) had ulcerative colitis (UC), 35 (61%) Crohn's disease (CD) and 5 (9%) unclassified IBD (uIBD). Up to 35 (61%) were male and the mean age at diagnosis was 10.2 $\pm$ 4.1 years. A total

of 18 (32%) were currently on biological treatment and 45 (79%) on immunosuppressants. The disease location in CD patients was L3 (Paris classification) in 22 (63%) and L4a in 13 (37%). Only 2 (6%) showed perianal involvement. From the UC patients, 11 (65%) were E4. A delayed growth was observed in 6 (10%), all CD patients. At diagnosis, 37 (65%) were HBV-vaccinated, 13 of them (35%) had a serological response and 22 (59%) had no response. Amongst the latter, 18 were re-vaccinated and 9 (50%) had a documented serological response.

Up to 34 patients (60%) were MMR-vaccinated and 13 (38%) showed a complete response. Only 6 patients could be re-vaccinated. Up to 30 (52%) showed chickenpox immunization. Only 4 of the non-immunized patients could be vaccinated and all of them responded to a single dose. Regarding CMV and EBV, 17 and 16 patients (46 and 43%) were IgG positive respectively, all of them were IgM negative. Patients with CD were more likely to need HBV re-vaccination than other IBDs ($p < 0.05$). Regarding chickenpox, CD patients without growth delay (G0) needed less re-vaccination than those whose growth was affected (G1) ($p < 0.05$). However, UC patients with extensive disease (E4) needed less re-vaccination than those with limited disease ($p < 0.05$). Male patients seemed to be less likely to need re-vaccination, with no significant differences.

Conclusion: The serological assessment of vaccine-preventable diseases immunization yielded poor results. Remarkably, a high percentage of HBV and MMR vaccinated patients showed no response. CD patients tended to more likely need revaccination, especially in the most severe cases (G1). Surprisingly, severity was not related with vaccination response in UC. Our results suggest that less than half of the patients had been previously infected by CMV or EBV. Based on this, it seems reasonable to serologically check the immunization status in PIBD patients in order to, when appropriate, re-vaccinate before starting immunosuppressive therapies.

Disclosure: Nothing to disclose

P0418

PATIENTS WITH CROHN'S DISEASE HAVE MORE PSYCHOPATHOLOGY THAN THE NORMATIVE POPULATION, BUT LESS THAN PSYCHIATRIC OUTPATIENTS

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Introduction: The Brief Symptom Inventory (BSI) is a self-report instrument designed to measure psychological distress in sick and healthy populations (Derogatis, 1983). The scale is widely used to screen for psychopathology and as an outcome measure in studies of psychiatric and chronic medical patients, like Crohn's disease (CD) (Slonim-Nevo, 2016). However, normative data for BSI are lacking for patients with CD.

Aims & Methods: This study aimed to establish clinical norms for the BSI using a sample of CD patients in Israel where psychiatric disease was excluded. 430 adult patients (≥ 18 y) with CD were recruited consecutively from outpatient gastroenterology clinics and self-filled the BSI questionnaire. Their data were compared with normative data from the adult general Israeli population (Gilbar, 2002) and adult British psychiatric outpatients (Ryan, 2007). Group comparisons were performed using the Welch's

t-test or analysis of variance, depending of the number of groups. To account for multiple comparisons, statistical significance was set at $p < .01$.

Results: Demographic and medical characteristics (mean $\pm$ SD,%) of the cohort were: age 38.5 y ($\pm$ 14.4); women 58%; Jewish 96%; employed 65%; education 14.6 y ($\pm$ 3.0); economic status poor (20%), medium (48%) or good (32%); disease duration 9.0 y ($\pm$ 6.1). Compared with normative data from the general population (N=510, age 45.6 $\pm$ 8.6 y, women 51%) patients with CD reported higher general severity scores (0.90 vs. 0.72 out of 4-point scale, $t_{(429)}=4.18$, $p < .001$). Patients with CD also endorsed higher levels of symptomatology than the general population across six dimensions of psychopathology: anxiety, depression, interpersonal sensitivity, obsessive-compulsive, phobic anxiety and somatization. In contrast, compared with psychiatric out-patients in the UK (N=378, women 67%, age 36.7 y ($\pm$ 11.7), patients with CD had significantly lower levels of mental health symptoms, shown by the general severity scores (1.65 vs. 0.90, $t_{(377)}=13.9$, $p < .001$) and across all BSI subscales. In terms of patient characteristics, no significant gender differences in BSI dimensions were found in patients with CD, with the exception of somatization; women had higher levels of somatic symptoms compared with men (1.05 vs. 0.83, $t_{(417)}=2.58$, $p=.010$). CD aged ≥ 60 endorsed lower levels of general psychological distress compared with younger age groups (0.60 vs. 0.94 for CD aged 30-59 and < 30 , $F_{(2,427)}=5.25$, $p=.005$). Similar age differences were found on the subscales of depression, anxiety, phobic anxiety, interpersonal sensitivity and psychoticism. Interestingly, levels of psychological symptoms did not differ with respect to disease duration. Finally, statistically significant differences were found between economic status categories in each of the BSI scales and the general severity scores; CD patients reporting poor economic status had more severe levels of general distress, followed by those with medium and then good economic status (1.43 vs. 0.85 vs. 0.61, $F_{(2,421)}=43.5$, $p < .001$).

Conclusion: Current results confirm the link between CD and elevated mental health symptoms. Specifically, patients with CD reported worse mental health symptoms than the general population; yet these levels were still lower than those of psychiatric outpatients. Additionally, the study findings suggest that poor economic status and younger age are associated with increased risk of distress in CD. Finally, the findings highlight the importance of using appropriate norms when assessing clinically significant levels of psychological distress in patients with CD.

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Disclosure: Nothing to disclose

P0419

ASSESSMENT OF THE NUTRITIONAL STATUS OF PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS ACCORDING TO DISEASE ACTIVITY

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Introduction: To determine the nutritional status in patients with inflammatory bowel disease (IBD) and its possible relationship with the activity of the disease.

Aims & Methods: We performed a cross-sectional and descriptive study of patients with previously diagnosed or suspected IBD under 18 years who underwent upper endoscopy (EGD) and colonoscopy, blood tests, stool cultures and MR Enterography (MRE) in a 15 days range, from October 2018 to February 2020. The clinical and endoscopic situation were assessed with the activity indices PUCAI/PCDAI/shPCDAI and the activity scores UCEIS/Mayo/SES-CD respectively, according to the underlying pathologies. The statistical analysis was performed with the SPSS® software, and we considered a P value < 0.05 statistically significant.

Results: We recruited 21 patients and 12 of them were males (57%). A total of 12 patients had Crohn's disease (CD) (57%), 3 had ulcerative colitis (UC) (14%), 6 had IBD unclassified (IBDu) (28%). The age at the time of the evaluation was 14.2 ± 0.7 years and the progression time of the disease was 3.9 ± 0.6 years.

A total of 16 patients showed clinical remission (76%), and 6 of them (28%) also had endoscopic and histological remission. Eight patients were receiving biological treatment (38%).

Rotavirus, adenovirus, Clostridium difficile toxin analysis and stool culture were performed in 14 patients, all of them were negative. The mean weight was (mean values $\pm$ SD) 55.7 ± 20.71 kg, the mean size was 159.1 ± 15.0 cm and the mean BMI was 21.5 ± 5.6 . A total of 7 patients (58%) had malnutrition, 3 (14%) were overweight and 2 (10%) were obese. We found no significant differences in BMI according to the underlying diagnose.

The results of the blood analysis with nutritional profile were (mean values $\pm$ SD) : folic acid 12.3 ± 7.2 ng/ml, vitamin B12 455.2 ± 200.6 pg/ml, ferritin 36.9 ± 16.7 ng/ml, total protein 7.6 ± 0.5 g/dl, albumin 4.4 ± 0.4 , prealbumin 22.7 ± 7.0 mg/dl, retinol binding protein 2.2 ± 1.0 mg/dl, vitamin A 0.3 ± 0.1 mg/L, effective vitamin E 4.6 ± 0.7 mg/g, 25(OH) vitamin D 20.1 ± 6.2 ng/ml, vitamin B1 6.1 ± 1.2 mcg/dL, vitamin B6 28.3 ± 9.8 ug/L, IFG-1 312.1 ± 124.1 ng/ml, IGF-1 3.4 ± 0.6 μ g/ml, PTH 54.9 ± 2.7 , Selenium 88.7 ± 23.1 , Zinc 99.4 ± 9.3 , copper 96.0 ± 11.5 ug/dL.

The albumin levels showed no statistically significant correlations with the PCDAI/ shPCDAI/PUCAI values. We found a significant negative correlation between the IGF-1 levels and the SES-CD values, and between prealbumin levels and Mayo score values ($p < 0.05$). However, no significant correlations were found between other nutritional values and endoscopic scores.

We found a significant negative correlation between the BMI values and the shPCDAI ($p < 0.05$), but no significant correlation was found with the clinical score used for UC and IBDu (PUCAI). No differences in analytical markers or BMI were found between patients receiving biological treatment and those who were not.

Conclusion: More than half of the teenager patients with IBD showed some kind of nutritional disturbance, and they did not seem to be related to the underlying diseases. The analytical nutritional markers which related more closely to the endoscopic activity were IGF-1 and prealbumin. The

alteration of the clinical score was related to alterations in the BMI in CD but not in the UC patients. The pIBD patients are a vulnerable population and their nutritional status should be carefully monitored by their physicians.

Disclosure: Nothing to disclose

P0420

VITAMIN D AND BONE MINERAL DISEASE IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Vitamin D has been linked to various processes in human tissues that extend far beyond its established action on calcium homeostasis and bone metabolism. It has also immuno-modulator (in particular anti-inflammatory) function. Although high prevalence of vitamin D deficiency and bone mineral disease was reported in Inflammatory Bowel Disease (IBD) patients, it is not clear if this is a cause or a consequence of the disease.

The aim of the present study was to determine epidemiological and clinical variables potentially associated with bone mineral alterations and vitamin D deficiency.

Aims & Methods: We conducted a prospective not randomised study of 184 patients with IBD (115 with CD and 69 with UC). 47% were women. Vitamin D metabolites, parathyroid hormone and biochemical markers of bone metabolism were measured in blood and urine.

Results: Vitamin D deficiency (defined as 25-hydroxyvitamin D3 < 30 nmol/l) was present in 80,8% of patients with CD and 81,8% with UC. PTH level was elevated in 17% of CD and 12,9% of UC (p 0.261). Furthermore, CD patients had over two times lower mean concentration of 25 hydroxyvitamin D3 compared with UC patients (p 0.359). Interestingly phosphate in urine in CD group was lower than in UC group (p 0.004), what indicates that CD patients are more vulnerable to secondary parathyroidism. Mean calcium level was 2.40 in CD group and 2.48 (p 0.554). Moreover, bone turnover parameter CTX indicating bone resorption was elevated in UC group then CD (p 0.293), whilst osteocalcin was comparable in both groups (p 0.095).

Conclusion: Hypovitaminosis D is common in IBD patients and more profoundly expressed in population of CD patients what may influence on the course of the disease. Therefore, patients with IBD are at high risk of development of secondary hyperparathyroidism and bone resorption what should be especially considered in management of this group of patients.

Disclosure: Nothing to disclose

P0421 WITHDRAWN

P0422

HIGH CORRELATION OF THE QUANTUM BLUE® RAPID ASSAY WITH HPLC TANDEM MASS SPECTROMETRY FOR INFLIXIMAB THERAPEUTIC DRUG MONITORING

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Introduction: A successful and cost effective infliximab therapy for patients suffering from chronic inflammation such as inflammatory bowel disease (IBD) is jeopardized if the drug is not adjusted within an ideal therapeutic window¹. Several methods allow for quantitative determination of infliximab serum levels to achieve therapeutic drug monitoring (TDM) and guide clinical decision-making. TDM rapid testing enables immediate result reporting and therapy adjustments without delay. Still, comparability of different infliximab assays is a common issue which needs to be addressed. Here, we report high comparability of the Quantum Blue® Infliximab rapid test to the highly precise HPLC tandem mass spectrometry (LC-MS/MS) method established at Mayo Clinic (USA)².

Aims & Methods: Hundred and twenty-seven de-identified blood serum samples from patients receiving infliximab were measured using LC-MS/MS (SCIEX API 5000) at Mayo Clinic² and the Quantum Blue® Infliximab lateral flow based rapid test. The obtained infliximab concentrations from both methods were compared by Passing-Bablok linear regression and Bland-Altman analysis. Furthermore, precision assessment of the Quantum Blue® Infliximab assay was conducted using the LC-MS/MS spiked human serum quality control samples at infliximab target concentrations of 2.5, 8 and 21 µg/mL, n=25 replicates.

Results: The sample values obtained with the Quantum Blue® Infliximab rapid test showed comparability to the values gained with the LC-MS/MS method. Passing-Bablok regression analysis revealed a correlation coefficient of $r = 0.965$ and a slope of 0.7632 when infliximab concentrations ranged from 1 to 70 mcg/mL. Bland-Altman analysis revealed a mean difference in the obtained values of -2.12 µg/mL towards the LC-MS/MS reference method. The precision assessment for the Quantum Blue® Infliximab assay showed 14.2% CV for target level 2.5 µg/mL, 19.3% CV and 19.1 %CV for target levels 8 and 21 µg/mL respectively. Further, the two methods present an overall analytical agreement of 91.3%, 88.2% and 81.1% at commonly used, pathology dependent decision points of 1 µg/mL, 3 µg/mL and 5 µg/mL correspondingly.

Conclusion: The Quantum Blue® Infliximab rapid test correlates very well with the LC-MS/MS method for infliximab trough level determination. Therefore, the rapid test fulfills high comparability to the LC-MS/MS method and represents a unique and modern analytical tool, for fast time-to-result and simplicity of usage in a more patient near medical environment.

References: 1. Vande Casteele, N. et al., 2015, Trough Concentrations of Infliximab Guide Dosing for Patients with Inflammatory Bowel Disease, *Gastroenterology* 148: 1320 - 1329 2. Willrich, M. A. et al., 2015, Quantitation of infliximab using clonotypic peptides and selective reaction monitoring by LC-MS/MS. *Int Immunopharmacol.* 28(1): 513-20

Disclosure: Nothing to disclose

P0423

BIOPSIES FROM ULCER EDGE YIELD HIGHER HISTOLOGICAL ACTIVITY SCORES THAN BIOPSIES NEXT TO ULCER IN ACTIVE ULCERATIVE COLITIS

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Introduction: Histological disease activity is being increasingly assessed in clinical trials in ulcerative colitis (UC) as a treatment outcome. However, the appropriate location for biopsy procurement relative to ulcers in UC is unknown.

Aims & Methods: We aimed to determine the location for biopsy collection in the presence of ulcers in UC which yields the highest histopathological score.

Methods: This prospective cross-sectional study at University medical center Ljubljana between 2018 and 2020 enrolled adult patients with a histologically confirmed diagnosis of UC and ulcers in the colon (Mayo endoscopic score 3). Biopsy specimens were obtained at three different distances from ulcers (edge of the largest ulcer (1); at a distance of one open forceps (7-8 mm) from the edge of the ulcer (2); at a distance of three open forceps (21-24 mm) from the ulcer in non-ulcerated mucosa (3); further referred to as locations 1, 2 and 3 respectively). Colonoscopies were video-recorded and endoscopic disease activity was assessed using Mayo endoscopic score by a single experienced central reader who also confirmed the correct biopsy procurement and subsequent eligibility of samples for statistical analysis. Histopathological disease activity was assessed using Robarts Histopathology Index (RHI) and the Nancy Histological Index (NHI) by a single blinded expert gastrointestinal pathologist. Statistical analysis was performed using mixed effects models with location as fixed effects and patients as random effect to account for within-subject correlations among locations (1, 2 and 3).

Results: A total of 23 patients met the eligibility criteria. After assessment by the central reader 4 patients were excluded (in three cases biopsies were not taken at the correct location relative to the ulcer, in one patient endoscopic activity was scored with Mayo endoscopic score 2) and 19 patients were included in the statistical analysis (mean age was 50.6 years with a range of 20-90 years, 58% females). Decreasing trends with distance from the ulcer edge ($P < 0.0001$) were observed in both histological disease activity scores. Biopsies procured from the edge of the ulcer (location 1) yielded a higher histopathological score using NHI and RHI compared to biopsies procured at location 2 in 3 in the non-ulcerated colonic mucosa ($P \leq 0.001$). Although a trend was observed towards decreased histological disease activity scores in location 3 relative to location 2, these differences were not statistically significant. Mean histological disease activity scores according to biopsy location are summarised in Table.

Location	1 (ulcer edge)	2 (7-8 from mm edge)	3 (21-24 mm from edge)
Robarts Histopathology Index	24.05 (5.19) 1, 3	12.53 (5.98) 4	9.95 (5.28)
Nancy Histological Index	3.74 (0.45) 2, 3	2.74 (1.05) 5	2.47 (0.84)

[Mean histological disease activity scores according to biopsy location]

(Values in parentheses represent Standard Deviation. Pairwise comparison with location 2, ¹ $P < 0.0001$ and ² $P = 0.001$; or location 3, ³ $P < 0.0001$, ⁴ $P = 0.071$ and ⁵ $P = 0.172$).

Conclusion: In active UC biopsies from ulcer edge yielded higher histopathological scores than biopsies next to ulcer. These findings could be implemented in clinical trials assessing histological disease activity as a treatment outcome.

Disclosure: Nothing to disclose

P0424

PATIENT REPORTED OUTCOMES, PARTIAL MAYO SCORE AND SCCAI ARE EQUALLY ACCURATE IN PREDICTING MUCOSAL HEALING IN UC: PRELIMINARY RESULTS FORM A PROSPECTIVE STUDY

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Introduction: Optimal management of patients with ulcerative colitis (UC) requires the accurate assessment of disease activity. Endoscopic evaluation is considered the gold standard approach, but it is invasive.

Aims & Methods: We aimed to determine how strong patient reported outcomes, clinical scores and symptoms correlate with endoscopy for assessment of disease activity in UC patients.

136 patients were included prospectively and consecutively (age: 48 (IQR: 38-61) years, duration 12 (4-19) years, 63 females, 53.7% extensive disease, 40.4% on biologicals) at the time of the colonoscopy. The 2 item patient reported outcome (PRO), partial Mayo, Simple Clinical Colitis Activity Index (SCCAI), Mayo endoscopic subscore (MES), Baron and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) scores were calculated. C reactive Protein (CRP) and fecal calprotectin (FCAL) was available in 58.1 and 33.8% of patients. 20.7% had clinical flare, treatment was escalated in 17.8% of patients. Sensitivity, specificity, PPV and NPV values were calculated, ROC analysis and K-statistics were performed.

Results: Rectal bleeding (RBS), stool frequency (SF) subscore of 0, or total PRO2 remission (RBS 0 and SF ≤ 1), partial Mayo (≤ 2) and SCCAI (≤ 2.5) remission were similarly associated to mucosal healing defined by MES (0 or ≤ 1) or Baron (0 or ≤ 1) scores (Table 1). PRO2 remission ($AUC_{MES/Baron0-1} = 0.747/0.715$, $AUC_{MES0-1/Baron0-1} = 0.867/0.863$), SF ($AUC_{MES0/Baron0} = 0.731/0.703$, $AUC_{MES0-1/Baron0-1} = 0.851/0.839$), RBS ($AUC_{MES0/Baron0} = 0.708/0.685$, $AUC_{MES0-1/Baron0-1} = 0.828/0.835$) partial Mayo ($AUC_{MES0/Baron0} = 0.792/0.755$, $AUC_{MES0-1/Baron0-1} = 0.917/0.903$) and SCCAI ($AUC_{MES0/Baron0} = 0.738/0.724$, $AUC_{MES0-1/Baron0-1} = 0.908/0.880$) were similarly associated with mucosal healing in a ROC analysis. There was a strong association between MES and Baron ($K = 0.798$), while moderate agreement between UCEIS and MES ($K = 0.451$) or Baron ($K = 0.499$) scores. Agreement between CRP and clinical remission or endoscopic healing (MES/Baron) was poor ($K \sim 0.2$), while agreement between FCAL (>100 or >250) and RBS-PRO2 remission ($K_{>250} = 0.56-0.61$) or MES/Baron 0 was moderate to good ($K_{>100} = 0.54-0.53$ and $K_{>250} = 0.50-0.54$).

Conclusion: We found no difference across accuracy of RBS, SF, PRO2, partial Mayo and SCCAI in predicting endoscopic healing. A strong association was found with high PPV for MES/Baron ≤ 1 and high NPV for MES/Baron 0. FCAL, but not CRP was associated to clinical and endoscopic remission.

References: Sensitivity Specificity PPV NPV PRO RBS 0 vs MES 0 97.5% 43.3% 72.2% 92% PRO RBS 0 vs MES ≤ 1 96.1% 67.7% 90.7% 84% PRO RBS 0 vs Baron 0 97.3% 39% 66.7% 92% PRO RBS 0 vs Baron ≤ 1 92.7% 70.8% 93.5% 68% PRO SF 0 vs MES 0 93.8% 50.9% 74.3% 84.4% PRO SF 0 vs MES ≤ 1 91.2% 74.2% 92.1% 71.9% PRO SF 0 vs Baron 0 93.2% 45.8% 68.3% 84.4% PRO SF 0 vs Baron ≤ 1 87.2% 75% 94.1% 56.2% PRO2 remission vs MES 0 96.2% 47.2% 73.3% 89.3% PRO2 remission vs MES ≤ 1 95.1%

74.2% 92.4% 82.1% PRO2 remission vs Baron 0 95.9% 42.4% 67.6% 89.3%
PRO2 remission vs Baron ≤ 1 90.8% 75% 94.3% 64.3% partial MAYO vs MES
0 98.8% 43.4% 72.5% 95.8% partial MAYO vs MES ≤ 1 99% 74.2% 92.7%
95.8% partial MAYO vs Baron 0 98.6% 39% 67% 95.8% partial MAYO Baron
 ≤ 1 94.5% 75% 94.5% 75% SCCAI vs MES 0 96.2% 45.3% 72.6% 88.9% SCCAI
vs MES ≤ 1 96.1% 74.2% 92.5% 85.2% SCCAI vs Baron 0 95.9% 40.7% 67%
88.9% SCCAI vs Baron ≤ 1 91.7% 75% 94.3% 66.7%

Disclosure: Nothing to disclose

P0425

UCEIS IS ASSOCIATED WITH PRO2, PARTIAL MAYO AND SCCAI REMISSION IN UC: PRELIMINARY RESULTS FORM A PROSPECTIVE STUDY

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Introduction: Optimal management of patients with ulcerative colitis (UC) requires the accurate assessment of disease activity. Endoscopic evaluation is considered the gold standard approach, but it is invasive.

Aims & Methods: We aimed to determine the operating characteristics of the Ulcerative Colitis Endoscopic Index of Severity (UCEIS), to quantify the cut off most closely correlated with clinical remission or activity and determine agreement with the Mayo endoscopic subscore (MES), Baron score, clinical scores and biomarkers. 136 patients were included prospectively and consecutively (age: 48 (IQR38-61) years, duration 12 (4-19)years, 63 females, 53.7% extensive disease, 40.4% on biologicals) at the time of the colonoscopy. Ulcerative Colitis Endoscopic Index of Severity (UCEIS) Mayo endoscopic subscore (MES), Baron scores were calculated, as well as the 2 item patient reported outcome (PRO), partial MAYO, Simple Clinical Colitis Activity Index (SCCAI). CRP and fecal calprotectin (FCAL) was available in 58.1 and 33.8% of patients. 20.7% had clinical flare, treatment was escalated in 17.8% of patients. ROC analysis and K-statistics were performed and Spearman's correlation was calculated.

Results: UCEIS was strongly associated to PRO2 SF (AUC:0.866), RBS (AUC:0.921), PRO2 combined remission (AUC:0.905), partial MAYO (AUC:0.956) and SCCAI (AUC:0.907) remission in a ROC analysis. A UCEIS of ≤ 3 was identified as the best cut-off to identify RBS subscore of 0, or total PRO2 remission (RBS 0 and SF ≤ 1), partial MAYO (≤ 2) and SCCAI (≤ 2.5) remission, while a UCEIS ≥ 4 identified active disease frequently needing change in medical therapy. A moderate agreement was found between UCEIS and MES (K=0.451) or Baron (K=0.499) scores. Correlation between FCAL and UCEIS (coeff:0.743, p< 0.0001) was strong, while modest only with CRP (coeff:0.333, p=0.01).

Conclusion: A UCEIS was strongly associated with clinical remission defined as PRO2, SF, RBS, partial Mayo or SCCAI with best agreement with RBS and partial Mayo remission. A UCEIS of ≤ 3 was identified as a cut-off for quiescent disease, while a UCEIS ≥ 4 identified active disease, which can support clinical decision-making based on endoscopic findings. Agreement between UCEIS and FCAL was strong, while agreement with UCEIS and MES/Baron scores was moderate.

Disclosure: Nothing to disclose

P0426

DO PSEUDOPOLYPS INCREASE FECAL CALPROTECTIN IN PATIENTS WITH ULCERATIVE COLITIS IN CLINICAL AND ENDOSCOPIC REMISSION?

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Introduction: Fecal calprotectin, a calcium-binding protein mainly derived from neutrophils, is widely accepted as a useful marker of intestinal inflammation. FC levels correlate significantly with disease activity in patients with inflammatory bowel disease. However, FC levels can increase as a consequence of different factors such as drugs, age, infections or other inflammatory bowel conditions (e.g. diverticulitis). Recent studies suggest that also pseudopolyps can be associated with increased FC in patients with ulcerative colitis (UC).

Aims & Methods: The aim of our study was to assess whether pseudopolyps increase FC levels in patients with UC in endoscopic remission.

Methods: A single-center, observational cohort study was designed. Adult patients with endoscopic diagnosis of quiescent UC between January-2017 and March-2019 were included; FC levels prior to colonoscopy were recorded. Quiescent UC was defined as endoscopic Mayo score of 0. Any modification of therapy between FC quantification and colonoscopy, any NSAIDs intake before FC test and any enteric infection 4 weeks before or after FC quantification were considered exclusion criteria. Data are shown as percentage, median, interquartile range (IQR) and mean $\pm$ standard deviation as appropriate. Wilcoxon rank-sum (Mann-Whitney) test was performed to assess potential differences of FC levels between patients with and without pseudopolyps.

Results: 133 patients were included (mean age 56.6 $\pm$ 15.01 years, 57.9% female). About 63% of patients were non-smokers. 51 patients had extensive UC, 50 left-sided UC and 29 had proctitis. Most of them (57.8%) were under 5-ASA monotherapy. 34 patients had pseudopolyps, 13 of whom presented pseudopolyps from the cecum to the rectum. Median FC was 43 μ g/g (IQR 20-129) in patients with pseudopolyps and 29 μ g/g (IQR 12-93) in those who had no pseudopolyps (p=0.10). Regarding the location of the pseudopolyps, median FC was 92 μ g/g (IQR 36-178) in patients with pseudopolyps in 4 sections of colon (ascending colon, transverse colon, descending colon and rectum) and 34 μ g/g (IQR 12-110) in patients with ≤ 3 sections affected by pseudopolyps (p=0.17). Median FC was 43 μ g/g (IQR 20-883) in those patients who had large pseudopolyps (≥ 10 mm) compared to 62 μ g/g (IQR 19-119.5) in the group with smaller pseudopolyps (p=0.55). During 6 months of follow up after colonoscopy, 3 patients had a flare and all of them had a FC <100 μ g/g.

Conclusion: Pseudopolyps do not significantly increase FC levels in patients with UC in endoscopic remission.

Disclosure: Nothing to disclose

P0427

BIOMARKERS OF ELASTIN DEGRADATION DIFFERENTIATE BETWEEN CLINICALLY INACTIVE AND ACTIVE DISEASE IN UC PATIENTS

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Introduction: In ulcerative colitis (UC) the state of chronic inflammation results in increased matrix metalloprotease (MMP) and serine protease activity, which effectively leads to a higher degree of intestinal tissue remodeling, including components of the extracellular matrix (ECM). One of these components is elastin a matrix protein of the interstitial matrix in the lamina propria and submucosa, providing tissue resilience and elasticity.

Aims & Methods: We sought to investigate whether elastin degradation in UC patients were associated with disease activity and severity, potentially enabling patient differentiation based on elastin degradation.

29 UC patients and 29 healthy donors (HDs) were included in this study. Disease activity was determined according to the partial Mayo score (pMayo>1) and the Mayo Endoscopic Score (MES). Disease severity and extension was assessed using the Montreal classification. Disease severity was additionally assessed using the Trulove and Witt's (TW) clinical score. The biomarkers of elastin degradation included: MMP-7 (ELM-7) cathepsin-G (EL-CG), and proteinase-3 (ELP-3), measured in serum by ELISA. Receiver operating characteristic was applied, discriminating between biomarker levels of UC patients and HDs, using the hybrid Brown/Wilson method for confidence interval computation.

Results: All three elastin degradation biomarkers were able to significantly discriminate between HDs and UC patients based on their clinical scores assessed by TW, pMayo, and Montreal classification. Utilizing the TW score, the ELP-3 biomarker significantly discriminated between the HDs and moderate to severe patients (AUC 0.842, $p < 0.001$) with a sensitivity of 75% and specificity of 82.8%. Both ELP-3 and EL-CG discriminated between HDs and patients (AUC 0.852, $p < 0.001$, and 0.783, $p < 0.01$) with an active disease based on the pMayo score with a sensitivity and specificity of 76.9%/82.8%, and 76.9%/76.9%, respectively.

The ELM-7 biomarker could discriminate between patients in remission and an active disease (AUC 0.792, $p < 0.05$) according to the Montreal classification with a sensitivity of 63.6% and specificity of 92.9%.

Endoscopic assessment using the MES score, ELP-3 could discriminate between HDs and moderate to severe patients (AUC 0.825, $p < 0.001$) with a sensitivity of 76.9% and a specificity of 82.8% (table 1).

Biomarker	TruLove and Witt's: HD vs. Moderate to Severe		
	AUC(95% CI)	p	Sens/Spec
ELP-3	0.842(0.70-0.98)	0.0007	75/82.8
pMayo: HD vs. Active			
ELP-3	0.852(0.72-0.98)	0.0003	76.9/82.8
EL-CG	0.783(0.62-0.94)	0.0038	76.9/76.9
Montreal: Remission vs. Active			
ELM-7	0.792(0.60-0.98)	0.0138	63.6/92.9
MES: HD vs. Moderate to Severe			
ELP-3	0.825(0.68-0.96)	0.0009	76.9/82.8

[Diagnostic power of the elastin degradation biomarkers based on clinical and endoscopic score]

Conclusion: Data presented in this study demonstrates the association between biomarker levels of proteolytic degradation of elastin and the disease activity in UC patients. Furthermore, the data revealed a role for the biomarkers in discriminating between UC patients and HDs. Especially the protease-3 derived biomarker, ELP-3, could discriminate the HDs from patients with a clinically active disease or UC patients with a moderate to severe endoscopic disease activity. Thus, utilizing these minimally invasive elastin degradation biomarkers could serve as surrogate markers for monitoring of disease activity and potentially aid the differentiation of patients with an active disease from patients in remission or with a lower disease activity for UC.

Disclosure: JHM: full time employee at Nordic Bioscience; TMJ and MAK, full time employees and stock-holders at Nordic Bioscience; VD, MB, AB, and ŽK: no disclosures

P0428 WITHDRAWN

P0429

MEASUREMENT OF FAECAL INFlixIMAB IN ULCERATIVE COLITIS POTENTIALLY INCREASES THE ACCURACY OF DISEASE MONITORING AND EVALUATION OF THERAPEUTIC RESPONSE

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Introduction: Faecal drug concentration is not routinely measured as per therapeutic drug monitoring strategies in inflammatory bowel disease (IBD) patients receiving anti-TNF therapy. However, our previous research work suggested the potential role of faecal drug monitoring of anti-TNF agents since active disease may be present in spite of normal serum anti-TNF levels.

Aims & Methods: The aim of the present study was to examine the correlation between faecal infliximab (IFX) concentration and objective activity markers of IBD and to evaluate the cut-off value of faecal drug concentration in the respect of faecal calprotectin in patients treated with maintenance IFX therapy. Consecutive patients with IBD receiving maintenance IFX therapy at 1st Dept. of Medicine, University of Szeged were enrolled in the present study. Demographic parameters, data on concomitant medications, C-reactive protein (CRP) levels and clinical disease activity indices were recorded. Faecal samples were obtained before the subsequent IFX infusion. Faecal calprotectin and IFX concentrations were determined with ELISA. The correlations of faecal IFX concentration with demographic parameters, concomitant steroid and immunomodulator therapy, CRP and faecal calprotectin were statistically assessed.

Results: Eighty-three IBD patients were enrolled. Female/male ratio was 47% - 53%. Sixty-six point three% of the patients were diagnosed with Crohn's disease and 33.7% with ulcerative colitis (UC). Mean disease duration was 14.7 years at the time of analysis. Mean duration of IFX therapy was 39 months. Twenty-eight point nine% of the patients received escalated IFX therapy. Mean faecal calprotectin concentration was 535.4 µg/g. Mean faecal IFX concentration was 1.014 ng/ml. Faecal IFX concentration did not show correlation with faecal calprotectin, CRP or activity indices. However, faecal IFX concentration was significantly higher in UC patients who presented with a faecal calprotectin level higher than 250 and 300 µg/g ($p \leq 0.001$ and $p = 0.002$). Cut-off value of faecal IFX was 0.62 ng/ml at

faecal calprotectin concentration of 250 µg/g (AUC 85%). No association was shown between faecal IFX levels and gender, disease type, disease duration, disease extent or location, IFX dosage and concomitant steroid or azathioprine use.

Conclusion: IFX concentration in the faeces proved to be significantly higher in patients with active UC defined by faecal calprotectin, the most accurate activity marker of the disease. Simultaneous determination of faecal anti-TNF and faecal calprotectin concentration is supposed to have higher benefit in the evaluation of response to IFX therapy.

Disclosure: Nothing to disclose

P0430

IMPROVEMENT OF INTESTINAL ULTRASOUND PARAMETERS WITHIN 12 WEEKS AFTER TREATMENT INDUCTION IN CD AND UC PATIENTS - FIRST INTERIM ANALYSIS OF THE TRUST BEYOND STUDY

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Introduction: Both ulcerative colitis (UC) and Crohn's disease (CD) exhibit a progressive and destructive nature which necessitates regular, objective disease monitoring. This can be challenging as clinical symptoms often poorly correlate with objective signs of inflammation. Both the TRUST and TRUST&UC study demonstrated a good correlation of changes in intestinal ultrasound (IUS) parameters, e.g. bowel wall thickness (BWT), of laboratory parameters and of endoscopy, respectively [1, 2].

For UC patients, we recently demonstrated a significant reduction in BWT as early as 2 weeks after treatment intensification. However, the predictive value of changes in IUS for the long-term treatment outcome is not well established.

Aims & Methods: The TRUST BEYOND study is an ongoing, prospective, observational, multi-centre study in patients with active CD or UC, in which a biologic- or JAK-therapy is initiated. The aim of this study is to evaluate the predictive value of IUS parameters, assessed at week 12 after treatment intensification, for the long-term disease outcome after 1 year (e.g. clinical, endoscopic, and steroid-free response). For this interim analysis, 50 patients with a total amount of 211 analyzed segments and a documented T1 visit after 12 weeks were included. The following colon segments were assessed at each visit: sigmoid colon, descending colon, transverse colon, ascending colon. The terminal ileum was only assessed in CD patients.

Results: Fifty patients with active disease (21 CD-patients and 29 UC-patients) and increased bowel wall thickness (BWT, sigmoid colon > 4 mm; descending colon, transverse colon, ascending colon, terminal ileum, all > 3 mm) at T0 were enrolled so far at 37 sites until January 2020. Patients were predominantly male (64.0%, n = 32) with a median age of 35 years (30.8 - 56.2) and a median disease duration of 8.53 years (2.03 - 11.53). In 54.8% (121 segments) of the assessed segments, a pathological BWT was present at baseline. Further IUS pathologies including an amplified Colour Doppler signal indicative of an increased vascularity were documented in 50.0% of the patients (n = 25). At T0, 54.0% (n = 27) of the patient population were naïve to therapy with biologics/JAK-inhibitors.

12 weeks after induction of biologic/JAK therapy, the percentage of segments with a pathological BWT was significantly reduced (from 54.8% (121 segments) at T0 to 24.0% (53 segments) at T1, p < 0.001). Improvements in Colour Doppler signal and in further IUS pathologies were also observed in the patient population at T1 (amplified Colour Doppler signal: from 50.0% (n = 25) to 14.0% (n = 7), p < 0.001; loss of stratification: from 40.0% (n = 20) to 22.0% (n = 11), p = 0.035). The improvement of the IUS results was accompanied by a significant improvement in disease activity (SCCAI: from 8.0 to 1.0 points; HBI: from 11.0 to 2.0 points).

Conclusion: In this interim analysis of the TRUST BEYOND study, the documented IBD-patients demonstrated a significant improvement in IUS results as well as in clinical parameters 12 weeks after treatment intensification. The results confirm the tremendous value of IUS in monitoring IBD patients in routine medical practice.

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P0431

HOSPITAL RE-ADMISSIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE- WHAT ARE THE RISK FACTORS?

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Introduction: Early re-admission after hospitalisation for an inflammatory bowel disease (IBD) flare is a negative quality indicator and causes unnecessary healthcare expense. Scoring systems to predict IBD readmissions have been shown to be ineffective. We aimed to describe the IBD re-admission rate at our hospital and investigate the risk factors.

Aims & Methods: Retrospective study of patients admitted to a London-based district general hospital under the gastroenterology team with a flare of inflammatory bowel disease between 2015 and 2018. Characteristics including but not limited to demographics, disease type, length of stay during index admission, biochemistry and biologic use were recorded. Hospital software (Sunquest Integrated Clinical Environment, Medway) was used to identify patients re-admitted at 30 and 90 days after discharge. Multivariate logistic regression was performed.

Results: 138 patients were admitted with an IBD flare during the study period (74 (53.6%) Crohn's disease (CD), 56 (40.6%) ulcerative colitis (UC), 8 (5.8%) IBD-U). Median age 33.5 (IQR 26 - 52), 71 (51.4%) female. Median length of stay was 4.5 days (IQR 1.8 - 8). 36 (26%) patients were taking a biologic. Re-admissions occurred within 30 days in 19 patients (13.7%) and within 90 days in 30 patients (21.7%). Multivariate logistic regression showed that a raised CRP on discharge was associated with re-admission.

For every increased unit of CRP by one there was an increased risk of readmission by 1.1 times ($p=0.05$). Patients aged 22-39 were significantly less likely to be readmitted (OR: 0.38, $p=0.015$). Male patients were significantly more likely to be readmitted (OR: 2.52, $p=0.05$).

Conclusion: The 30 day and 90 day re-admission rate for our IBD population is just over 10% and 20%, respectively. CRP at discharge is significantly associated with both 30 and 90 day re-admission. After adjusting for confounders; CRP, age older than 40 and male gender were associated with re-admission to hospital. We advise caution in discharging IBD patients with raised inflammatory markers. Close follow up within a few days of discharge would be appropriate in this high risk sub-group.

Disclosure: Nothing to disclose

P0432

CHANGE IN THE EXPRESSION OF SERPIN E1, A POTENTIAL NEW DISEASE ACTIVITY MARKER, REFLECTS THERAPEUTIC RESPONSE IN INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) occurs as a consequence of an abnormal immune response generating an unbalance between pro- and anti-inflammatory signalling. Analysis of the cytokine profiles in the view of different cytokine targeting or immunosuppressive therapy may open up new therapeutic targets and may reveal biological profiles that distinguish responders from nonresponders before initiating therapy.

Aims & Methods: The aim of the present study was to determine cytokine profile of IBD patients and identify cytokines with predictive potential. IBD patients with clinically active disease were enrolled in the study. Blood, faecal and biopsy samples were obtained from IBD patients and healthy controls. Control group consisted of non-IBD subjects who underwent colonoscopy. Biopsies were taken from inflamed and non-inflamed part of colon of IBD patients. Total protein and mRNA were isolated from blood and biopsy samples. Cytokine Array was used to analyse cytokine expression patterns. Serum, mucosal and faecal SerpinE1 levels were measured by ELISA and qRT-PCR.

Results: We determined the cytokine profile of 36 biopsy samples (14 patients and 4 controls). As expected, in the control samples no cytokines were detected, which potentially play role in the inflammatory process. In samples from IBD patients, remarkable discrimination between the inflamed, or non-inflamed areas was detected. Serpin E1 was presented in every inflamed biopsy samples. Therefore, we performed further measurements regarding Serpin E1 expression. Mucosal expression of Serpin E1 differed significantly in healthy subjects compared to IBD patients with active disease (0 vs. 24.06 pg/mg, $p=0.02$). After the introduction of immunosuppressive and/or biological therapy remarkable decrease was observed in mucosal expression of Serpin E1 in patients who responded to the therapy ($p=0.06$) compared to non-responders ($p=0.15$). Moreover,

mean value of mucosal Serpin E1 concentration did not differ significantly in healthy subjects compared to responders (5.7 vs. 0 pg/mg, $p=0.12$). In the non-responder samples the fold changes of Serpin E1 gene expressions were significantly ($p=0.018$) higher than in the responders. Lowest expression of Serpin E1 gene was measured in control samples, whereas the highest in the untreated, inflamed biopsy samples. Serpin E1 could be detected in both serum and faecal samples, however, due to low samples numbers, statistical analyses could not be performed yet.

Conclusion: Our results suggest that mucosal SerpinE1 expression reflects endoscopic activity of IBD, which could be used as promising marker of disease activity and therapeutic response. Correlation of Serpin E1 expression between the blood, faeces and the bowel mucosa would open up new possibilities in non-invasive disease monitoring of IBD.

Disclosure: Nothing to disclose

P0433

NUTRITIONAL STATUS AND DISEASE ACTIVITY IN CROHN'S DISEASE: PRELIMINARY DATA

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Introduction: Malnutrition is a highly prevalent and crucial complication of Crohn's Disease (CD), even in patients in remission; nevertheless assessment and treatment of malnutrition is rarely integrated into management plans. Body Mass Index (BMI) and Malnutrition Universal Screening Tool (MUST) are widely used, but not exempt of limitations.

Aims & Methods: The aims of this study were to investigate (1) the prevalence of malnutrition in an outpatient sample of CD patients, using the most frequent and recommended nutritional tools in clinical practice (2) the existence of any relationships between nutritional and clinical status in patients with CD, and (3) the reliability and validity of different methods of nutritional assessment in patients with CD in an ambulatory setting. Cross-sectional, observational study that took place in the IBD outpatient clinic at University College Hospital between March and June 2019. Demographic (gender, ethnicity, age and smoking status), and disease activity data (Harvey Bradshaw Index, Montreal Classification, past surgical history, current and past medication) were collected. Nutritional assessment was performed, using weight, height, BMI, MUST, Mid-upper arm circumference (MUAC) and Hand Grip Strength (HGS). Additionally, blood biomarkers [Haemoglobin, Platelets, Ferritin, C - reactive protein (CRP), Vitamin D, B12, and Folate] were recorded.

Results: 86 consecutive CD patients were included (38 female; mean age 38.5±15.3 years; 19 Asian, 67 of white ethnicity; 62 non-smokers, 13 smokers and 11 ex-smokers). Statistically significant positive associations were found between clinical activity (HBI) and MUST ($r=0.426$, $r^2=0.18$, $p<0.05$), CRP ($r=0.282$, $r^2=0.079$, $p<0.05$) and Platelet values ($r=0.24$, $r^2=0.079$, $p<0.05$). A significant positive association was found between MUST and CRP ($r=0.29$, $r^2=0.08$, $p=0.0049$) and negative between MUST and BMI ($r=0.43$, $r^2=0.19$, $p=0.000002$). No significant association was found between the other parameters collected. In the sub analysis comparing active (HBI≥5; n=40) vs remission group (HB<5; n=46), there was a trend for a lower mean

HGS in the active group (29.58 ± 11.89 vs 33.94 ± 12.66 ; $p=0.1$). MUST score 0 was more prevalent in patients in remission compared with active ($n=31$ vs $n=22$; $p<0.005$) and MUST score 1 was more common in the active group ($n=13$ vs $n=7$; $p<0.005$). The prevalence of malnutrition was 12.5% in the active group, and 17.3% in the remission group, when calculated with MUST; and 22.5% in the active group and 8.69% in the remission group by BMI criteria.

Conclusion: Malnutrition rates are high in patients with CD, even in remission. HGS was lower in the active group while MUST was negatively associated with BMI. Malnutrition screening and assessment should be included routinely in IBD clinical practice. Further data are being collected based on body composition.

Disclosure: Nothing to disclose

P0434

HIGHER ANXIETY LEVELS AND A NEUROTIC PERSONALITY ARE ASSOCIATED WITH NON-COMPLIANCE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: To make medical therapy of inflammatory bowel disease (IBD) successful medication adapted to disease activity and patient's expectations is crucial. However, every therapy may fail, if patient compliance is low. Here we investigate personality traits such as anxiety, depression and neurotic personality disorders and their impact on compliance in IBD patients.

Aims & Methods: 291 IBD patients filled in an anonymous questionnaire on IBD itself, on disease activity (HBI or pMS, respectively), QoL (SIBDQ) and sociodemographic factors. Standardized tests were used to determine psychological differences between compliant and non-compliant patients: Hospital Anxiety and Depression Scale (HADS), State-Trait-Anxiety Inventory (STAI), Social Support Questionnaire (F-SozU), Complaints-list (BL-R'), NEO-Five-Factor Inventory (NEO-FFI).

Results: 138 (47.2%) male and 151 (52.8%) female patients, 183 (62.9%) with Crohn's disease and 108 (37.1%) with ulcerative colitis completed the questionnaires. 219 (77.9%) IBD patients reported to be compliant and 62 (22.1%) reported to be not compliant with doctor's orders.

Patients reporting non-compliance were in general younger ($n=61$, 38.3 ± 12.8 vs. $n=217$, 43.4 ± 15.5 years, $p=0.008$) even at the age of the diagnosis of IBD ($n=61$, 24.9 ± 9.5 vs. $n=214$, 30.4 ± 13.6 years, $p=0.026$) and ordered to take a higher amount of pills or suppositories per day ($n=61$, 2.8 ± 4.6 vs. $n=219$, 1.7 ± 3.1 pills/supp. / day, $p=0.048$). Investigating personality traits and compliance we found some significant differences as given in table 1. Non-compliant patients have higher scores on depression scale in HADS ($p=0.034$), a higher number of general complaints in BL-R' ($p=0.003$) and lower scores for social support in F-SozU ($p=0.029$).

Both the values of the HADS anxiety ($p=0.001$) and in STAI state ($p=0.002$) and trait anxiety scales ($p<0.001$) are significantly higher in non-compliant patients. Non-compliant patients showed significantly higher values in personality trait neuroticism ($p=0.001$) in NEO-FFI. Compliant patients stand out due to significantly higher values in the characteristics extraversion ($p=0.014$), agreeableness ($p=0.008$) and conscientiousness ($p=0.003$).

	compliant			non-compliant			p-value
	n	mean	SD	n	mean	SD	
depression (HADS)	217	4.3	3.6	61	5.6	4.2	0.034
anxiety (HADS)	217	6.0	3.8	61	7.8	3.8	0.001
state-anxiety (STAI)	210	37.9	11.2	61	43.1	12.5	0.002
trait-anxiety (STAI)	212	38.5	10.7	61	44.7	11.8	<0.001
complaints (BL-R')	212	18.7	9.3	62	22.2	9.6	0.003
social support (F-SozU)	213	4.3	0.7	60	4.0	0.8	0.029
neuroticism (NEO-FFI)	212	19.1	8.0	62	23.3	8.8	0.001
extraversion (NEO-FFI)	212	27.3	7.5	62	24.7	6.3	0.014
agreeableness (NEO-FFI)	212	31.3	5.6	62	29.2	5.5	0.008
conscientiousness (NEO-FFI)	212	34.9	6.4	62	32.2	5.7	0.003

[table 1: psychological differences of compliant/non-compliant patients (t-test $p<0.05$; n=number; SD=standard deviation)]

Conclusion: Results on HADS depression and anxiety and STAI state anxiety scale show depression and anxiety are key factor associated with non-compliance. Results in STAI trait anxiety and NEO-FFI indicate that non-compliant patients more often have an anxious and/or neurotic personality. Based on our results, at least non-compliant IBD patients should be questioned about their concerns and fears regarding therapy in order to better respond to them and possible increase compliance and therapy success.

Disclosure: Nothing to disclose

P0435

ALFA-1 ANTITRYPSIN AS A REGULATING MARKER OF INFLAMMATION IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: The determination of permeability enhancing protein (BPI) and protease inhibitor $\alpha 1$ -antitrypsin ($\alpha 1$ -AT), which play an important role in the pathogenesis and regulation of the inflammatory process in inflammatory bowel diseases, can be used as diagnostic and prognostic markers in patients with ulcerative colitis (UC).

Aims & Methods: To determine the level of $\alpha 1$ -antitrypsin in the blood serum and faeces of patients with UC to assess the activity of inflammation in the intestine.

Thirty-four patients with UC were examined (average age - 39, min. - 19, max. - 61 years) with different disease activity according to the Mayo activity index. In the blood serum and faeces, $\alpha 1$ -AT ($\alpha 1$ -Antitrypsin Clearance ELISA Immunodiagnostik, Germany) and IgG to the penetration enhancing protein (BPI) (Bactericidal permeability-increasing protein) were determined. Software Statistics 6.0 was used

Results: In the blood serum of patients with UC, $\alpha 1$ -AT deviations from 235 to 4203 $\mu\text{g/L}$ were detected (the norm is 900-1800 $\mu\text{g/L}$). An increase in $\alpha 1$ -AT concentration was detected in 19 patients ($2743.6 \pm 1051.2 \mu\text{g/L}$), in 7 - the parameter remained within the normal range ($1272 \pm 532.3 \mu\text{g/L}$), in 8 - $\alpha 1$ -AT concentration decreased ($305.8 \pm 146.3 \mu\text{g/L}$). Antibod-

ies to BPI were detected in 18 patients with continuous severe disease ($r = 0.43$). An increase in the concentration of $\alpha 1$ -AT in faeces was observed in 17 patients with UC (from 90 to 792 $\mu\text{g/g}$ of faeces) (normal 25–35 $\mu\text{g/g}$ of faeces), that indicates impaired permeability of the intestinal wall. In 1 patient with steroid-resistant pancolitis, the increase in $\alpha 1$ -AT reached 905 $\mu\text{g/g}$ of faeces, in 9 patients with UC of moderate severity was detected an increase in $\alpha 1$ -AT ($95.2 \pm 43.1 \mu\text{g/g}$ of feces). A low level of $\alpha 1$ -AT ($15.2 \pm 5.6 \mu\text{g/g}$ feces) was determined in 7 patients with mild UC.

Conclusion: An increase in $\alpha 1$ -AT in the blood serum and faeces of patients with UC is a prognostic marker of high activity of inflammation, which may reflect the clinical course of the disease and could be used as a predictor of the development of UC complications in future.

Disclosure: Nothing to disclose

P0436

NOVEL SERUM SOLUBLE MARKERS OF HISTOLOGICAL HEALING IN ULCERATIVE COLITIS

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Introduction: The recent introduction of a commercial panel of soluble biomarkers that can predict endoscopic healing may support the monitoring and management of Crohn's disease, reducing the need of repeated endoscopy. ¹ Achieving histological remission (HR) is currently considered to be an important target in ulcerative colitis (UC). ²

Aims & Methods: The aim of this study was to identify serological markers of HR in patients with UC and determine their diagnostic accuracy individually and in combination to predict HR.

We enrolled 40 UC patients referred to a tertiary academic centre for colonoscopy as part of standard of care. Demographic data, serum samples and histologic data: Robarts Histopathology Index (RHI) and Nancy index score were collected. Concentrations of these biomarkers were compared with the histology at the time that the patients underwent colonoscopy with advanced enhancement technologies and targeted biopsies. Histological healing was defined as Nancy ≤ 1 and RHI ≤ 3 .

A total of 55 soluble analytes relevant to inflammation or shown to be altered in IBD were measured in serum using Procartaplex luminex assays (ThermoFisher). Finally, 24 analytes that were detected in more than 40% of patients were selected in downstream modelling and used to train a logistic regression model.

Results: We identified Brain-Derived Neurotrophic Factor (BDNF) and Macrophage Inflammatory Proteins (MIP-1 α) that when combined together showed the highest predictive power for predicting RHI ≤ 3 and Nancy ≤ 1 with an area under receiver operating characteristic curve (AUROC) of 0.82 (95% CI, 0.69–0.97). When we investigated analytes separately for predicting the same outcome, univariate logistic regression was significant for two other markers: Leukemia Inhibitory Factor (LIF) and Vascular Cell Adhesion Molecule 1 (sVCAM1) showing higher values associated with the lack of healing. The AUROC was 0.74 for LIF, (95% CI: 0.591–0.89) and 0.72 for sVCAM1 (95% CI: 0.53–0.90).

Conclusion: BDNF, MIP-1 α , LIF and sVCAM may be promising markers to assess histological healing in UC patients. Replication in larger cohorts of patients is now required.

OMN* and LJ* - equal authors

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Disclosure: Nothing to disclose

P0437

ANTI-DRUG ANTIBODIES DETECTED IN THE PRESENCE OF ADEQUATE INFLIXIMAB DRUG LEVELS IN IBD PATIENTS IN CLINICAL REMISSION HAVE LIMITED CLINICAL SIGNIFICANCE

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Introduction: Immunogenicity, with the development of antibodies-to-infliximab (ATI), increases drug clearance and can lead to loss of infliximab (IFX) response in inflammatory bowel disease (IBD) patients. The reporting of ATI is variable between commercial assays, with some assays having high sensitivity for low-titre antibodies. Uniform thresholds for clinically relevant antibody titres are lacking. In this context, it is unclear how ATI affect treatment outcome when adequate trough IFX concentrations are present and ATI are detected.

Aims & Methods: We aimed to assess the impact of ATI detected in the presence of adequate IFX levels on the outcome of IFX therapy in IBD patients in clinical remission. As a pilot project, a proactive therapeutic drug monitoring (TDM) strategy was utilised in our unit with IFX and ATI levels, assessed at trough, in all IBD patients receiving IFX therapy using a commercial assay IDKmonitor® (Immunodiagnostik, Bensheim, Germany). Baseline demographics data were collected on all patients. Patients were grouped based on disease activity status with remission defined by any one of the following criteria: faecal calprotectin $< 150 \mu\text{g/g}$, C reactive protein $< 5 \text{ mg/L}$, absence of active disease at endoscopy performed within 3 months of TDM assessment or physician's impression of disease remission at the time of TDM assessment. Trough IFX and ATI levels were documented for all patients. An adequate trough IFX level was defined as a trough IFX concentration $> 3 \mu\text{g/mL}$, with low IFX levels defined as those $< 3 \mu\text{g/mL}$. ATI positivity was considered as an ATI concentration $> 10 \text{ AU/mL}$. Receiver operating characteristic (ROC) analysis was performed to evaluate the classifying performance of ATI concentration for low IFX levels. Survival analysis was performed to determine IFX persistence in patients with adequate IFX levels and positive ATI. Follow up TDM assessments, where available, were documented to determine changes in ATI concentration over time in patients with adequate IFX levels.

Results: N=108 patients were included ([median age 36 years, 46% were female, 36% ulcerative colitis, 60% Crohn's disease, 4% IBD-U] 35% were receiving concomitant immunomodulators. N=59 (56%) of patients were in remission at the time of TDM assessment. 44%, 30% and 26% of patients had IFX levels $< 3 \mu\text{g/mL}$, 3–7 $\mu\text{g/mL}$ and $> 7 \mu\text{g/mL}$ respectively. Median [range] ATI concentration was 11 AU/mL [0–800]. ATI positivity occurred in 25%, 19% and 8% of IFX groups with levels $< 3 \mu\text{g/mL}$, 3–7 $\mu\text{g/mL}$ and $> 7 \mu\text{g/mL}$ respectively. There was a weak inverse correlation between trough ATI and IFX concentration, pearson correlation coefficient -0.24, $p=0.01$. ATI concentration performed poorly as a classifier of low IFX levels, AUC 0.568 (95% CI 0.41–0.72), $p=0.39$. 83% (15 of 18) of IBD

patients in remission with adequate IFX levels and positive ATI remained on IFX for the duration of follow up with a mean (95%CI) cumulative time on IFX of 111.2 weeks (95% CI 105.1 - 117.3). In this group, there was no significant change in ATI titre comparing index with follow up TDM assessments ($p=0.14$).

Conclusion: ATI positivity in the presence of adequate IFX levels is common when proactive TDM assessments are performed in IBD patient populations. For patients in clinical remission ATI positivity in the presence of adequate IFX levels has limited clinical significance. Care should be taken to avoid unnecessary therapy alterations in this patient subgroup when proactive TDM strategies are being utilized.

Disclosure: Nothing to disclose

P0438

INVESTIGATING THE ASSOCIATIONS BETWEEN PATIENT REPORTED OUTCOMES AND FAECAL CALPROTECTIN IN ULCERATIVE COLITIS: THE DISCORDANCE BETWEEN "GUT FEELING" AND IBD -"CONTROL"

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Introduction: The IBD Control questionnaire is a validated, patient reported outcome measure (PROM) designed to measure inflammatory bowel disease (IBD) activity. However, data on its performance compared to objective measures of inflammation are scarce.

Aims & Methods: Here, we prospectively evaluated the diagnostic yield of IBD Control and its sub-scores (IBD control-8 and IBD-control-VAS), compared to faecal calprotectin (FCP) levels, in patients with ulcerative colitis (UC). Patients with UC attending IBD clinics completed a series of validated questionnaires including the IBD-control questionnaire, the Rome IV diagnostic questionnaire for functional bowel disorders, and submitted a sample for FCP. On IBD Control questionnaires; quiescent UC is defined as IBD-control-8 sub-score ≥ 13 and IBD-control-VAS ≥ 85 . FCP levels ≤ 250 ug/g were considered as inactive disease. IBD-control data were compared to FCP levels using simple linear regression analyses.

Results: 152 UC patients (mean age 51 ± 1.2 years, $n=66$ male) completed the study. Mean IBD control-8 subscore was 9.6 ± 0.5 , and mean IBD control-VAS was 60.7 ± 2.7 , whilst mean FCP level was 338.2 ± 40.7 . There were statistically significant correlations between FCP levels and IBD control data (FCP and IBD control-8: $R=-0.29$, $R^2=0.09$, $P=0.0002$; FCP and IBD control-VAS: $R=-0.36$, $R^2=0.13$, $P<0.0001$), although these correlations were weak. Interestingly, the diagnostic yield for active IBD using IBD-control questionnaire data was 84/152 (55%), however only 53/152 (34%) had FCP ≥ 250 . Of the 31 patients who met IBD-control criteria for active disease but had normal FCP, most patients met the Rome IV diagnostic criteria for at least one functional bowel disorder (IBS $n=15$, functional constipation $n=5$ and faecal incontinence $n=17$).

Conclusion: These data are amongst the first to confirm an association between PROMs for IBD activity and objective measures of inflammation. However, when used exclusively, PROMs may over estimate disease activity, and do not account for patients with overlapping functional bowel disorders which may mimic active inflammation in quiescent disease.

Disclosure: Nothing to disclose

P0439

COST EFFECTIVENESS OF A PROACTIVE THERAPEUTIC DRUG MONITORING STRATEGY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE RECEIVING INFLIXIMAB

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Introduction: Proactive therapeutic drug monitoring (TDM) is widely used in clinical practice, however, has not been clearly demonstrated to result in improved anti-TNF therapy outcomes compared with clinically-based dosing strategies. While the use of proactive TDM incurs additional assay-related costs this strategy may be cost-effective due to TDM-driven anti-TNF therapy dose de-escalation and discontinuation.

Aims & Methods: We aimed to assess whether use of proactive-TDM is a cost-effective strategy in routine clinical practice. As a pilot project, a proactive TDM strategy was utilised in our unit with infliximab (IFX) levels and antibody-to-infliximab (ATI) levels, assessed at trough, in all inflammatory bowel disease (IBD) patients receiving IFX therapy. Baseline demographics including IFX dosing schedules and use of concomitant immunomodulators were documented.

Patients were grouped based on disease activity status with remission defined by any one of the following criteria: faecal calprotectin < 150 $\mu\text{g}/\text{mg}$, C reactive protein < 5 mg/L , absence of active disease at endoscopy performed within 3 months of TDM assessment or physician's impression of disease remission at the time of TDM assessment.

Trough IFX and ATI levels were documented for all patients. Patients with IFX levels outside the therapeutic range of 3 - 7 $\mu\text{g}/\text{mL}$ had IFX therapy dosing adjusted as appropriate. IFX dose adjustments were not protocolised and were at attending physicians discretion. IFX dosing regimens following proactive TDM were documented and the net effect on IFX infusions number over the subsequent year extrapolated. Increase or decrease in drug-related costs on an annualised basis were then estimated.

Results: $N=108$ patients were included ([median age 36 years, 46% were female, 36% ulcerative colitis, 60% Crohn's disease, 4% IBD-U) 35% were receiving concomitant immunomodulators. 56% of patients were in remission at the time of TDM assessment. 44%, 30% and 26% of patients had IFX levels < 3 $\mu\text{g}/\text{mL}$, 3 - 7 $\mu\text{g}/\text{mL}$ and > 7 $\mu\text{g}/\text{mL}$ respectively. IFX levels were significantly lower in patients with active disease compared with those in remission ($p=0.008$). Following proactive TDM assessment, 37%, 11%, 36%, 13%, 2% and 1% of patients had no treatment change, therapy discontinuation, interval shortening, interval lengthening, dose increase and dose decrease respectively. Cost-effectiveness analysis focused on patients in remission ($n=59$).

The use of proactive TDM-based IFX dosing resulted in a projected annualised reduction of 19.5 and 28.5 infusions due to IFX discontinuation and interval lengthening respectively; the projected annualised increase in infusions was 39.1 and 4.3 due to IFX interval shortening and dose increase respectively. This resulted in a net projected reduction of 4.7 IFX infusions per annum. Utilising publicly available list prices for originator and bio-similar IFX and accounting for TDM assay cost (2065 Euro), projected cost savings resulting from proactive-TDM use were 9105.0 and 6840.7 Euro per annum respectively.

Conclusion: Proactive TDM in IBD patients in remission resulted in a modest reduction in the projected annualised number of infusions in our unit with consequent minor drug-related cost savings. Proactive-TDM encouraged cost-effective prescribing of IFX, however, the effect was minor. The

frequency at which proactive TDM should be performed and whether subsequent rounds of proactive-TDM would continue to deliver similar cost savings is uncertain and requires further evaluation.

Disclosure: Nothing to disclose

P0440

SUBOPTIMAL VACCINATION ADHERENCE IN MOTHERS WITH INFLAMMATORY BOWEL DISEASE AND THEIR BIOLOGIC EXPOSED INFANTS

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Introduction: Patients with inflammatory bowel disease on biologic therapies have specific vaccine recommendations designed to mitigate risk of infection. Further, guidelines recommend the avoidance of live vaccines in all pregnant women and specifically in biologic exposed infants within the first six months of life due to the transplacental transfer of IgG1 based monoclonal antibody therapies. Determining vaccine guideline adherence is the first step towards optimizing vaccine safety and reducing morbidity. Therefore, we assessed vaccination rates in pregnant IBD patients on biologic therapies and their infants. Further, we evaluated the safety and efficacy of the live rotavirus vaccine in these potentially vulnerable infants. This may help guide future vaccine recommendations.

Aims & Methods: This was a prospective cohort study that enrolled pregnant mothers with IBD and their infants from a tertiary referral IBD and pregnancy specialty clinic. Using a provincial electronic database, individuals were linked to vaccination records. We included 144 biologic exposed (72.2% CD vs 27.8% UC) and 159 unexposed (44% CD vs 56% UC) pregnant mothers and their respective infants (n=120 and n=142) to determine vaccination adherence rates. Potential rotavirus vaccine adverse events and infant gastroenteritis rates were obtained for biologic exposed and unexposed infants to determine vaccine safety and efficacy.

Results: High rates of routinely recommended influenza, HBV, DTaP and MMR vaccines were seen in biologic exposed and unexposed women (77.8% vs 75.5%; 81.9% vs 74.2%; 81.9% vs 84.3%; 65.3% vs 76.1%). In comparison, vaccines with IBD specific indications such as HAV, Pneumovax and Prevnar had lower adherence rates in both biologic exposed and unexposed groups (52.8% vs 57.2%, p=0.44; 39.6% vs 15.7%, p<0.01; 36.1% vs 16.3%, p<0.01). When comparing biologic exposed and unexposed infants there were high compliance rates for recommended vaccines with no significant differences in DTaP-IPV-Hib, MMR, Men-C and Pneu-C (91.7% vs. 90.1%, p=0.67; 95.8% vs. 93.9%, p=0.32; 95.8% vs. 93.0%, p=0.32; 95.0% vs. 93.7%, p=0.64). Rotavirus (RV) vaccination rates (20% vs. 87%, p<0.01) were lower in biologic exposed infants but still received at high rates considering the recommendation to avoid live vaccine before 6 months of age. In regard to the RV vaccine, biologic exposed and unexposed infants had similar rates of potential vaccine associated adverse events (n=1/15, 6.6% vs n=6/78, 7.6%). The RV vaccine was associated with a significant reduction in severe gastroenteritis in biologic unexposed children when compared to unvaccinated infants (n=5/78, 6.4% vs n=3/11, 27.2%, p=0.02) with similar rates in biologic exposed infants (n=2/15, 13.3% vs n=6/59, 10.2%).

Conclusion: Better education around disease specific vaccine recommendations is required in women with IBD and their biologic exposed infants, given poor HAV, Prevnar, Pneumovax and rotavirus vaccine adherence. Further studies assessing drug levels and immunophenotyping of infants maybe useful in determining RV vaccine safety and efficacy.

Disclosure: Nothing to disclose

P0441

CORRELATION BETWEEN MICROBIAL MARKERS AND FAECAL CALPROTECTIN IN IBD PATIENTS

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Introduction: Crohn disease (CD) and Ulcerative colitis (UC) are characterized by episodes of exacerbations and remissions. Monitoring disease activity based on intestinal lesion is mandatory prior to any change in the therapeutic strategy. Colonoscopy is the gold standard technique to monitor the disease activity in IBD patients, but it is usually discarded because of costs and risk issues. The concentration of Faecal Calprotectin (FC) is widely used as a non-invasive marker of inflammation of the intestinal mucosa, allowing the assessment of the disease activity.

Recently, different studies have demonstrated that certain microbial species, part of intestinal microbiota which can be detected in stool samples, are capable of correlating with disease activity in CD and UC patients.

Aims & Methods: The purpose of this study was to analyse the correlation between these microbial indicators and the FC to monitor the disease activity in CD and UC patients.

FC levels were used to define inflammatory disease activity, the predetermined cut-off of 250 µg/g of faeces was used, higher values indicated an active inflammation and lower values indicated disease in remission. Two cohorts consisting of 61 patients of CD (25 with active inflammation and 36 with disease in remission) and 90 of UC (42 with active inflammation and 48 with disease in remission) were recruited by the Gastroenterology department of 4 Catalan hospitals. A sample of faeces was collected from each patient. FC and the following markers were quantified by qPCR: *Faecalibacterium prausnitzii* (Fpra), *Escherichia coli* (Eco), *Akkermansia muciniphila* (Akk), *Ruminococcus* sp. (Rum), *Bacteroidetes* (Bac) and *Methanobrevibacter smithii* (Msm) for each sample.

Results: The bacterial markers presented different behaviour depending on the disease analysed. The abundances of Eco and Bac were higher in CD with active inflammation compared to CD with remission. In contrast, no significant differences were found for Fpra, Akk, Rum, and Msm. Besides, a significant positive correlation between Eco abundance and FC levels (0,280, p=0.029) and a significant negative correlation between Msm and FC levels (-0,299, p=0.021) were observed.

According UC patients, while the abundance of Eco was higher in patients with active inflammation, the abundance of Rum was significantly less abundant. No significant differences were found for Fpra, Akk, Bac, and Msm. Moreover, we also observed a significant negative correlation between Rum and FC levels (-0,308, p=0.003, respectively).

Conclusion: The abundance of Eco and Msm in CD patients and the abundance of Rum in UC patients correlate to FC in order to determine inflammatory disease activity. So, these markers can also be an accurate discriminator of active disease in CD and UC patients.

Disclosure: Nothing to disclose

P0442

ANXIETY, DEPRESSION AND ALEXITHYMIC TRAITS IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS: CORRELATIONS WITH CLINICAL SYMPTOMS AND INFLAMMATION INDICES

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Introduction: Inflammatory bowel disease (IBD) patients commonly report high levels of psychological distress, including anxiety and depression symptoms. In addition, they appear to face significant difficulties in emotional awareness due to inborn deficits in emotional recognition and expression (alexithymic characteristics). However, it is unclear whether patients' personality characteristics and psychological burden may contribute to clinical symptomatology and disease activity. In this context, the current study's objective was to investigate any correlations between alexithymic traits, psychological distress, gastrointestinal symptoms severity and laboratory inflammation indices.

Aims & Methods: Adult IBD patients were enrolled to the study during their regular visit at the Outpatient Gastroenterology Department of the University Hospital of Patras, Greece. All participants were administered the Hospital Anxiety and Depression Scale (HADS), the Toronto Alexithymia Scale (TAS) and the PROMIS Gastrointestinal Symptoms Scales (PROMIS-GI). Blood samples were also collected to measure C-Reactive Protein (CRP) levels and Sedimentation Erythrocyte Rate (SER).

Results: 53 IBD patients entered the study, 28 (52.8%) males, with a mean age of 39 years (range: 19-74). 36 (67.9%) patients were diagnosed with Crohn's disease (CD) and 17 (32.1%) with ulcerative colitis (UC). 44.2% and 34.9% of participants reported clinically significant anxiety and depression symptoms, respectively. 49% of patients presented with increased alexithymic traits compared to the Greek general population. The most prevalent and severe symptoms reported by patients were gas and bloating (T-score: 55.27±10.99) and diarrhea (T-score: 53.87±8.93). Difficulties in emotional recognition were strongly correlated with the severity of nausea and vomiting ($r=0.406$, $p=0.003$), disrupted swallowing ($r=0.301$, $p=0.034$), constipation ($r=0.308$, $p=0.030$), belly pain ($r=0.322$, $p=0.021$), reflux ($r=0.339$, $p=0.015$) and gas and bloating ($r=0.324$, $p=0.026$). In a similar way, difficulties in emotional expression significantly correlated with the severity of nausea and vomiting ($r=0.445$, $p=0.001$). The presence of anxiety symptoms was also associated with the severity of nausea and vomiting ($r=0.373$, $p=0.014$), disrupted swallowing ($r=0.319$, $p=0.039$) and gas and bloating ($r=0.342$, $p=0.031$). No significant correlations were detected between anxiety, depression or alexithymia and laboratory inflammation indices (SER and CRP).

Conclusion: Alexithymic traits are quite prevalent in IBD patients and they frequently have to cope with increased levels of psychological distress. Anxiety symptoms and alexithymic characteristics, especially difficulties in emotional recognition, appear to be linked with the severity of gastrointestinal symptomatology.

Disclosure: Nothing to disclose

P0443

BIOMARKERS OF ELASTIN DEGRADATION IS ASSOCIATED WITH CLINICAL AND BIOCHEMICALLY ACTIVE DISEASE IN CROHN'S DISEASE

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Introduction: In Crohn's disease (CD) the extensive and potentially transmural inflammation results in increased activity of both matrix metalloproteases (MMPs) and serine proteases, causing a higher degree of intestinal tissue remodelling. In time the excessive tissue remodelling of the extracellular matrix, including the interstitial matrix protein elastin, could become detrimental resulting in loss of tissue function.

Aims & Methods: Therefore, we sought to investigate the association between biomarkers of elastin degradation and the disease activity in CD patients.

72 CD patients and 29 healthy donors (HD) were included in the study. Disease activity was determined according to the Crohn's disease activity index score (CDAI>150) and/or a fecal calprotectin (fCALP>250). Additionally, CD patients were endoscopically assessed according to the simple endoscopic score (SES) for CD. Different protease derived biomarkers of elastin degradation: protease-3 (ELP-3), MMP-7 (ELM-7), and cathepsin-G (EL-CG) was measured in serum by ELISA. Receiver operating characteristic was applied for evaluating the biomarkers ability to discriminate between CD patients and HDs, utilizing the hybrid Brown/Wilson method for computation of the confidence interval.

Results: The ELP-3, EL-CG, and ELM-7 biomarkers were all capable of discriminating between CD patients with an active disease and the HDs (AUC 0.768, $p<0.001$; AUC 0.668, $p<0.05$; AUC 0.683, $p<0.01$). Biomarker levels of protease-3 mediated degradation demonstrated the highest sensitivity and specificity of the three biomarkers (70.3%/72.4%). Furthermore, ELP-3 could discriminate CD patients with an inactive from active disease (AUC 0.713, $p<0.01$) with a sensitivity of 62.2% and specificity of 77.1%. ELP-3 was additionally able to discriminate HDs from CD patients with a moderate to severe endoscopic score (AUC 0.818, $p<0.001$).

Biomarker	CDAI/fCALP: HD vs. Active		
	AUC(95% CI)	p	Sensitivity/Specificity
ELP-3	0.768(0.66-0.88)	0.0002	70.3%/72.4%
EL-CG	0.668(0.54-0.80)	0.0197	54.1%/79.3%
ELM-7	0.683(0.55-0.88)	0.0089	62.2%/75.9%
CDAI/fCALP: Inactive vs. Active			
ELP-3	0.713(0.59-0.83)	0.0019	62.2%/77.1%
SES: HD vs. Moderate to Severe			
ELP-3	0.818(0.68-0.95)	0.0006	73.3%/72.4%

[Diagnostic power of the elastin degradation biomarkers based on clinical and endoscopic score]

Conclusion: In this study quantification of protease-3, cathepsin-G, and MMP-7 mediated degradation of elastin demonstrated a significant AUC in discriminating between HDs and CD patients both clinically and for ELP-3 also endoscopically. The protease-3 generated degradation fragment measured by the ELP-3 biomarker could discriminate using both the combined score of CDAI and fCALP levels as well as the endoscopic SES score.

Protease-3 is of particular interest in the setting of IBD due to its relationship with the neutrophil extracellular traps. As such, the data provides an indication of the beneficial use of these serum biomarkers as additional tools for disease monitoring in CD patients.

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P0444

PHYSICAL EXERCISE IS ASSOCIATED WITH BETTER BODY COMPOSITION TRAITS IN YOUNG ADULTS WITH CHILDHOOD-ONSET INFLAMMATORY BOWEL DISEASE

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Introduction: Patients with inflammatory bowel disease (IBD), both adults and children, are at increased risk of developing disturbed body composition. Physical exercise (PE) influences body composition positively. However, there is limited data on the extent to which young adults with childhood-onset IBD exercise. Further, there is little data on the association between physical exercise and body composition traits (bone mineral density (BMD), skeletal muscle, and body fat percentage (fat %)) in this patient group with chronic inflammation.

Aims & Methods: This study aims to investigate the extent to which young adults with IBD engage in physical exercise during the last year and the association between their amount of physical exercise and body composition traits.

A total of 72 young adults (24 female) with childhood-onset IBD (24 patients with Crohn's disease) and 1341 normative young adult controls answered questionnaires regarding PE in hours/week (h/w) in the last 12 months. Body composition traits were measured with dual X-ray absorptiometry (DXA) and presented as age and gender-adjusted Z-scores for skeletal muscle index (SMI, the weight of lean mass in arms and legs/m²), fat % and BMD. The patients were categorized in three groups according to the degree to which they engaged in PE;

- i) No PE (Patients, n=31; Controls, n=428);
- ii) Moderate PE, 1-4 h/w (Patients, n=19; Controls n=428);
- iii) High PE, ≥4 h/w (Patients, n=22; Controls, n=485).

Results for moderate PE not shown in the current abstract. Following statistical methods were used:

- i) differences of measurement variables between any two groups were tested with the Mann-Whitney U test,
- ii) multivariable regression analysis was used to estimate the independent association of IBD diagnosis and PE group and body composition traits.

Results: A total of 41 (57%) of patients with IBD engaged in PE during the last 12 months, while the corresponding data in the control group was 913 (68%), p=0.053. Patients who did not exercise at all had significantly lower median body composition traits Z-scores (SMI, fat %, BMD) than sedentary controls (Table).

In contrast, patients within the high PE had SMI and fat % in the same range as the controls who trained accordingly (Table). However, this patient group had lower BMD in total body and femoral neck than the corresponding control group, whereas spine BMD Z-scores did not differ (Table).

A diagnosis of IBD was negatively associated with all body composition trait variables, regardless of the PE group. Despite that, the patients with high PE had all body composition traits in line with the corresponding data for the median Z-score of all controls (SMI -0.09 [-0.8-0.65], fat % -0.20 [-0.78-0.52], total body BMD 0.00 [-0.68-0.65], spine BMD -0.08 [-0.73-0.64], femoral neck BMD -0.07 [-0.77-0.68], all p>0.05).

Body composition trait Z-score	No physical exercise		High physical exercise	
	Patients, n=31	Controls, n=428	Patients, n=22	Controls, n=485
SMI	-0.71 (-1.54-0.16)*	-0.53 (-1.14-0.25)	0.46 (-0.52-1.02)	0.46 (-0.52-1.02)
Fat %	0.66 (0.01-1.67)*	0.04 (-0.68-1.01)	-0.14 (-0.85-0.78)	-0.41 (-0.85-0.26)
Total body BMD	-1.09 (-1.59-0.15)*	-0.25 (-0.91-0.36)	0.04 (-1.03-0.64)*	0.31 (-0.38-0.99)
Spine BMD	-0.92 (-1.6-0.27)*	-0.26 (-0.87-0.32)	-0.28 (-1.26-0.33)*	0.34 (-0.41-1.12)
Femoral neck BMD	-0.56 (-1.61-0.36)*	-0.38 (-1.05-0.26)	-0.12 (-0.88-0.35)	0.30 (-0.47-0.98)

*p<0.05. SMI, Skeletal muscle index; BMD, Bone mineral density. Values are median (IQR)

[Table: Body composition traits in physical exercise groups]

Conclusion: In this study of young adults with childhood-onset IBD, a positive association was seen between physical exercise and better body composition traits. The study results support the view that increased emphasis should be on promoting physical exercise in young adults with inflammatory bowel disease.

Disclosure: Nothing to disclose

P0445

SEROLOGICAL BIOMARKERS OF INTERSTITIAL MATRIX AND BASEMENT MEMBRANE REMODELLING CORRELATES THE MODIFIED MAYO ENDOSCOPIC SCORE (MMES) FOR ULCERATIVE COLITIS

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Introduction: Endoscopy is a mainstay in ulcerative colitis (UC) for disease activity monitoring. The modified Mayo Endoscopic Score (mMES) for UC takes into account disease extent and hereby additional objectivity can be achieved for endoscopic assessment. However, endoscopic evaluation of the intestinal mucosa is time-consuming and inconvenient for the patients. Therefore, surrogate biomarkers for endoscopic examinations are warranted. The aim of this study was to evaluate serological neo-epitope biomarkers of type IV collagen degradation (C4M) and formation (PRO-C4), type III collagen degradation (C3M), type V collagen formation (PRO-C5) and macrophage activity (VICM) and their association with the mMES for UC.

Aims & Methods: Endoscopic disease activity was scored using mMES for the UC patients (n=63). Patients were stratified according to the disease activity severity based on mMES (remission=0-1, mild=2-4, moderate=5-6, severe>6). ELISA was applied for biomarker measurements (C4M, PRO-C4, C3M, PRO-C5 and VICM) in serum. Pearson correlations and one-way-ANO-

VA with FDR correction was applied for statistical analysis. A multivariate regression model was developed in order to combine the ECM biomarkers as a composite index. This model was correlated with the mMES and compared to FC and C-reactive protein (CRP) levels.

Results: All the biomarkers correlated to mMES (VICM: $r=0.35$, $P=0.0063$; PRO-C5: $r=0.33$, $P=0.009$; C3M: $r=0.32$, $P=0.011$; C4M: $r=0.28$, $P=0.0255$; PRO-C4: $r=0.25$, $P=0.044$). Stratification of the patients, revealed that VICM, C3M, and C4M serum levels was significantly elevated in UC patients with severe mMES compared to patients in remission (VICM: $P=0.0158$, C3M: $P=0.04$), mild disease activity (VICM: $P=0.0002$, C3M: $P=0.0049$, C4M: $P=0.0084$) and moderate disease activity (VICM: $P=0.0166$). Biomarkers that correlated significantly with the mMES were included in the multivariate regression model as a composite biomarker index. The biomarker model correlated significantly with mMES ($r=0.45$, $P=0.0002$) and the model was also able to discriminate between the different stages of disease activity ($P=0.0007$). FC correlated with mMES ($r=0.48$, $P=0.0001$), however CRP did not correlate with mMES.

Conclusion: The combined tissue-remodeling biomarkers correlated significantly with mMES for UC. The ECM serological biomarkers performed better than CRP, and equally good as FC. Thus, serological biomarkers of ECM remodeling, especially basement membrane degradation, interstitial matrix degradation and macrophage activity biomarkers may be used as surrogate markers for endoscopic disease activity assessment for UC.

Disclosure: JHM, MLO, TMJ, MAK, are full time employees at Nordic Bioscience. MAK and TMJ holds stocks in Nordic Bioscience

P0446

EMERGING ROLE OF IL-33/ST2 AND GUT MICROBIOTA AXIS IN PREDICTING MUCOSAL AND HISTOLOGICAL RESPONSE TO ANTI-TNF THERAPY IN ULCERATIVE COLITIS

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Introduction: It is now well-established that IL-33/ST2 axis and gut microbiota are important factors in the pathogenesis of IBD with a potential reciprocal influence. Recent evidence has shown that tumor necrosis factor (TNF) inhibitors (anti-TNF) are able to modulate the IL-33/ST2 axis as well as gut microbiota in inflammatory conditions. Anti-TNF are considered to be effective in inducing mucosal healing in patients with moderate-to-severe Ulcerative Colitis (UC).

Aims & Methods: The aim of our study was to explore the potential role of the IL-33/ST2 axis and gut microbiota in the mucosal healing process mediated by anti-TNF therapy in UC. Endoscopic MAYO score and Simpli-

fied Geboes score (GS) were calculated before the first anti-TNF infusion (T0) and after 6 weeks (T2). 26 UC patients (MAYO score at T0 ≥ 2 , GS ≥ 2 B), grouped into 14 mucosal and histological responders (MAYO score ≤ 1 , GS < 2 A) and 12 non-responders to anti-TNF at T2 (MAYO score ≥ 2 , GS ≥ 2 B) were enrolled. 10 healthy controls undergoing routine colonoscopy for tumor screening were also enrolled. At each time point, serum and fecal samples were collected. ELISA and western blot were performed to assess IL-33/ST2 protein levels and to evaluate protein isoforms, respectively. Intestinal biopsies were also taken from the rectum and IHC was done to evaluate mucosal IL-33/ST2 expression and localization. Genomic DNA was extracted from fecal samples and V3-V4 regions of the 16S rRNA gene were sequenced by MiSeq Illumina platform for microbiota characterization.

Results: IL-33 protein levels were significantly increased in responders vs. non-responders, both at T0 and T2. Among responders, IL-33 protein was slightly reduced at T2 vs. T0, while unchanged in non-responders. Interestingly, significantly higher levels of ST2 were found in responders vs. non-responders at T0, while no differences between groups were found at T2. Among responders, ST2 levels were dramatically reduced at T2 vs. T0.

No significant differences were found in non-responders at both time points. Healthy controls showed significantly lower levels of both IL-33 and ST2 compared with other groups. Full-length, bioactive IL33 (31 kDa), ST2L (76 kDa) and sST2 (52 kDa) were expressed in all experimental groups; the cleaved, less active form of IL33 (24 kDa) was increased in only non-responders vs. responders and healthy controls.

IHC confirmed these observations. In particular, IL-33 and ST2 staining was more intense within the inflamed and ulcerated mucosa of responders compared to non-responders at T0. After 6 weeks, ST2 staining was even more evident in responders, notably localized to the healed mucosa and in close proximity to areas of re-epithelialization. Little to no staining for both IL-33 and ST2 was present in healthy controls. Microbiota analysis showed an increased biodiversity at T0 in responders vs. non responders. At T0, non responders showed lower levels of Verrucomicrobia (Akermansia municipihila) and Firmicutes, with an increased abundance of Bacteroidetes vs. responders.

Conclusion: Our results suggest a possible role for IL-33/ST2 and gut microbiota axis in predicting endoscopic and histologic wound healing in patients with moderate-to-severe UC treated with anti-TNF. IL-33/ST2 axis and gut microbiota could thus represent a useful diagnostic tool to evaluate therapeutical options in IBD patients. Further studies are underway to determine mechanisms of action that support these findings.

Disclosure: Nothing to disclose

P0447

MEASUREMENT OF ULCERATED AND AFFECTED SURFACE OF THE COLON MAY PROVIDE MORE INSIGHT INTO RESPONSE COMPARED TO ENDOSCOPIC MAYO SCORE - A POST HOC ANALYSIS

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Introduction: The endoscopic Mayo score assesses the worst endoscopic lesions of ulcerative colitis. It may overlook overall changes of the affected colon due its emphasis on features such as ulceration and spontaneous bleeding. The objective of this analysis was to assess whether the evaluation of affected and ulcerated surface provides more data granularity of endoscopic changes during induction treatment.

Aims & Methods: Colonoscopies from the placebo and PTG-100 900mg dose group of the PROPEL study at week 0 and week 12 were assessed in back to back fashion by a single central unblinded reader. Endoscopic disease severity was scored by the endoscopic Mayo score as total, and segmentally for the descending colon, sigmoid colon, and rectum. In addition, ulcerated and affected surface were scored on a total and segmental level on an incremental scale from 0 to 10. Ulcerated surface summarized the surface involved by erosions and ulcers, and affected surface reflected the surface by erythema, erosions and ulcers. For our analysis endoscopic remission was defined by an endoscopic Mayo score of 0 or 1, and endoscopic response by an improvement of 1 point from baseline.

Results: In total, 30 patients were included. 5 (16.7%) achieved remission and 4 (13.3%) achieved response but not remission by endoscopic Mayo score. In patients with endoscopic remission and response, the changes in the composite affected and ulcerated surface were similar to the reductions observed in the Mayo score. In 21 non-responders by the endoscopic Mayo score, some changes could be discerned in the affected and ulcerated surface that were not reflected in the endoscopic Mayo score. In 8 patients, although the worst affected segment was not improved, there were improvements observed in other segments of the colon. The corresponding reduction in total affected surface for these 8 patients was a mean of 22.9% (range: 3%-66%). Four of these patients had reduction in their total ulcerated surface, with a mean reduction of 51.3% (range: 33-66%). The segment with most changes according to Mayo score was the rectum (9 patients). In these patients, a mean of 90.4% improvement in ulcerated surface was observed (range 50-100%). A mean of 61.1% improvement in affected surface was observed (range 10-100%).

Conclusion: Our findings show that the endoscopic Mayo score lacks data granularity to highlight all changes in ulcerated and affected surface in ulcerative colitis. A validation process of a score measuring affected and ulcerated surface should be initiated.

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P0448

THE DIAGNOSTIC PERFORMANCE OF A TRAINED PHYSICIAN VS. A PEDIATRIC RADIOLOGIST IN PERFORMING AN INTESTINAL ULTRASOUND IN CHILDREN WITH IBD

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Introduction: Training non-radiologists to perform an intestinal ultrasound (IUS) during the outpatient clinic visit with equal accuracy as a radiologist could accelerate clinical decision making in pediatric IBD patients. In this study we assessed whether a physician can be trained to perform an IUS, with an accuracy that is non-inferior to an experienced radiologist in children with IBD.

Aims & Methods: In this prospective cross-sectional study, consecutive children with IBD or suspicion of IBD, who needed to undergo an ileo-colonoscopy for regular care underwent an IUS within 7 days of this reference standard. IUS was performed by the physician and radiologist on the same day. Operators were blinded for each other's IUS results, for the outcome of the reference standards and for clinical disease activity parameters. Disease activity per bowel segment (ascending colon (AC) and transverse colon (TC)) was defined as a SPAUSS score >7(1), a SES-CD (Crohn's Disease (CD)) score of ≥1, or a Mayo score (Ulcerative Colitis (UC)) of ≥1. Inter-observer variability for bowel wall thickness (BWT) was assessed with Bland-Altman plots. The diagnostic performance of the trained physician and the pediatric radiologist was compared with the McNemar test.

Results: We included 27 patients (14 males, 18 CD, 5 UC, 3 no IBD, mean age 15 years (range 11-17)). A total of 8/24 had active disease in TI (in 3 TI was not intubated), 10/27 in AC and 11/26 in TC according to the reference

standard. The mean difference in BWT between the operators was -0.06 (SD:1.11, 95% CI: -2.23-2.11), 0.07 (SD:0.79, 95% CI -1.49 - 1.62), and 0.15 (SD: 1.21, 95% CI:-2.22 - 2.52) mm for TI, AC and TC respectively. There was no systematic difference. For AC and TC, a trend towards a higher sensitivity was noted when IUS was performed by the trained physician (AC: 40 vs. 25%, TC: 55 vs. 11%) although not significantly ($p=1.0$ and 0.13 respectively). Specificity was 100% for both observers in both segments. For TI, the trend was reversed: sensitivity was 25 vs. 75% and specificity 81 vs. 93% ($p=0.13$).

Conclusion: Our results suggest that a trained physician can perform an IUS with an accuracy that is non-inferior to an experienced radiologist in children with IBD, although sensitivity was low for both operators. More research on the most optimal cut-off value for IUS in pediatric IBD is needed.

References: 1: Kellar A, Wilson S, Kaplan G, DeBruyn J, Tanyingoh D, Novak KL. The Simple Pediatric Activity Ultrasound Score (SPAUSS) for the Accurate Detection of Pediatric Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr.* 2019;69(1):e1-e6.

Disclosure: Nothing to disclose

P0449

PROGNOSIS OF CROHN'S DISEASE PATIENTS RECEIVING ANTI-TNF THERAPY ACCORDING TO ENDOSCOPIC HEALING OR RADIOLOGIC HEALING

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Introduction: Endoscopic healing (EH) has been regarded as the therapeutic goal in treating patients with Crohn's disease (CD). Because CD is a transmural disease, combined EH and radiologic healing (RH) could be a more optimal therapeutic goal. However, prognosis of patients with CD according to EH and RH has not been sufficiently investigated.

Aims & Methods: We aimed to evaluate the prognostic differences between CD patients with EH and combined EH and RH (deep healing, DH) under treatment with anti-tumor necrosis factor agents. A total of 392 patients who received anti-TNF treatment more than one year and evaluated with radiologic studies (CT enterography or MR enterography) together with colonoscopy performed within 3 months between July 2017 and December 2019 were enrolled.

Patients were divided into 4 groups: DH, EH alone, RH alone, and non-healing (NH, neither EH nor RH). Poor outcomes defined by anti-TNF dose intensification, switch to other biologics or CD-related bowel resection were compared according to EH and RH status.

Results: A total of 114 (29.1%) patients showed DH, 59 (15.1%) had EH only, 41 (10.4%) had RH only, and 178 (45.4%) had NH. During follow-up (median, 18 months [interquartile range, 15-21]), a Kaplan-Meier analysis with a log-rank test showed a better prognosis of the DH group compared with the other groups ($P<0.001$). In particular, when compared between the DH group and the MH alone group, the prognosis of the DH group was better than MH alone group ($P=0.004$). In the multivariable analysis, elevated CRP, MH alone, TH alone, and NH were associated with an increased risk of poor outcomes (adjusted hazard ratio [aHR] 2.04, 95%

confidence interval [CI] 1.40[BDYE1] -2.97, $P<0.001$, aHR 3.65, 95% CI 1.44-9.29, $P=0.006$, aHR 3.07, 95% CI 1.11-8.47, $P=0.030$, and aHR 9.49, 95% CI 4.38-20.58, $P<0.001$, respectively) (Table 1).

Conclusion: CD patients with DH showed a better prognosis compared with EH alone or RH alone. Beyond EH, DH could be a new therapeutic goal for patients with CD.

	Univariable analysis	Multivariable analysis				
	HR	95% CI	P-value	aHR	95% CI	P-value
CRP ≥ 0.6 mg/dL	2.55	1.76-3.69	<0.001	2.04		<0.001
Healing						
Deep healing	Reference	Reference				
Endoscopic healing	3.47	1.37-8.81	0.009	3.65	1.44-9.29	0.006
Radiologic healing	3.25	1.18-8.97	0.023	3.07	1.11-8.47	0.030
Non-healing	10.59	4.89-22.90	<0.001	9.49	4.38-20.58	<0.001

aHR, adjusted hazard ratio; CI, confidence interval; CRP, C-reactive protein; HR, hazard ratio; TNF, tumor necrosis factor

[Table 1. Univariable and multivariable analysis for factors associated with poor outcomes]

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P0450

THE POTENTIAL ROLE OF PROCALCITONIN AS A NOVEL SERUM INFLAMMATORY BIOMARKER IN ULCERATIVE COLITIS (UC) AND CROHN'S DISEASE (CD)

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Introduction: Performance of serum biomarkers in predicting disease activity in inflammatory bowel disease (IBD) is usually suboptimal even though this can be improved by their inclusion in clinical activity scores. Serum procalcitonin has recently become integral to the diagnosis and management of severe bacterial infections, where it is used to guide antibiotic therapy. Its use in the management of intrabdominal sepsis and other infective complications of IBD is indisputable, however conflicting evidence exists as to whether procalcitonin could also be used as a marker of disease activity.

Aims & Methods: We carried out a single centre cross-sectional case-control study comparing serum procalcitonin with other serum biomarkers in IBD patients in remission (controls) and those with active disease (cases). Disease parameters, treatment prescribed and activity scores were recorded for all patients. HBI and SCCAI scores >5 and/or endoscopic evidence of active disease were used to distinguish between the two.

Results: 113 IBD patients were recruited between January and December 2019. Average age was 44.1 years for cases ($n=51$) and 45.5 years for controls ($n=62$). Gender distribution (Females: 49.0% cases, 53.2% controls)

and IBD type (UC: 58.8% cases, 64.5% controls) were also similar between the 2 groups. Mean HBI and SCCAI scores for cases were 7.7 and 6.6 and those for controls were 0.2 and 0.1 respectively. Mean procalcitonin values (ng/mL) were significantly higher in active UC or CD compared to controls (0.104 ± 0.058 vs 0.030 ± 0.006). Values exceeding 0.5ng/mL were encountered only twice, a CD patient with intrabdominal sepsis and a case of fulminant UC. The correlation of serum biomarkers with HBI and SCCAI is summarised in Table 1.

	HBI (CD)		SCCAI (UC)		IBD Cases (n=51)	
	Pearson	p value	Pearson	p value	R ²	
ESR (mm/h)	0.432	0.108	0.63	0.205	0.130	
CRP (mg/L)	0.376	0.17	0.68	<0.001	0.355	
Plt (x10 ⁹ /L)	-0.071	0.802	0.214	0.304	0.009	
WCC (x10 ⁹ /L)	-0.163	0.562	0.613	0.001	0.189	
Procalcitonin (ng/mL)	0.665	0.007	0.695	<0.001	0.445	

[Correlation of serum biomarkers with clinical scores (HBI and SCCAI)]

Procalcitonin was the serum marker that correlated the most with disease activity, followed by CRP and WCC. A cut off value for procalcitonin at 0.032ng/mL was able to predict severe disease with a sensitivity and specificity of 0.65 and 0.60 respectively. An arbitrary cut off of 0.1ng/mL (n=11) was able to predict need for hospital admission and administration of intravenous antibiotics with a PPV of 91.0%.

Conclusion: In our patient cohort procalcitonin was the most reliable marker of disease activity in both UC and CD. We hypothesise that routine use of procalcitonin could lead to more appropriate prescription and earlier commencement of intravenous antibiotics, when indicated. Since the majority of patients with active disease had values traditionally considered normal, different cut off values should be applied when using procalcitonin as a marker for IBD disease activity. Further research is required to understand the underlying pathophysiology and whether this could be due to subclinical bacterial translocation or whether it is derived from increased leukocyte activity observed in IBD.

Disclosure: Nothing to disclose

P0451

PROACTIVE INFLIXIMAB DRUG MONITORING INDUCES FECAL BIOMARKER REMISSION IN INFLAMMATORY BOWEL DISEASE

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Introduction: Increasing evidence supports the use of therapeutic drug monitoring (TDM) to improve clinical decisions in Crohn's disease (CD) and Ulcerative colitis (UC). There is less agreement upon the potential benefits of proactive TDM (pTDM).

Aims & Methods: To study the effects of pTDM of Infliximab (IFx) in inducing fecal biomarker remission and its relation to clinical outcomes. Patients completing IFx induction were prospectively assigned to a pTDM protocol. Before the 4th infusion and every 2 infusions, drug levels and anti-drug antibodies were measured using a drug sensitive assay (Thera-diag®, Lisa Tracker) and treatment was proactively escalated to a trough

level of 3-7 ug/ml (CD) or 5-10 ug/ml (UC). Fecal biomarker remission was defined as a fecal calprotectin < 250 ug/g. Endpoints included clinical remission, surgery, hospitalization, and treatment discontinuation at 2 years of follow-up.

Results: 83 patients were included in the study, 57.8% with Crohn's disease. Median baseline fecal calprotectin was 1246 ug/g (205-13710). Median IFx trough levels at week 14 (W14TL) were 4.2 ug/ml (0-20). Following the protocol, escalation over 2 years occurred in 74.7% of patients resulting in end of study IFx trough levels (2YTL) of 6.22 ug/ml (0-24.4). Fecal biomarker remission was achieved in 63.9% of patients (P = 0.17 between diseases). There was a higher correlation between target fecal calprotectin and 2YTL (r = -0.434, P < 0.001) than W14TL (r = -0.301, P = 0.006). There was no correlation between W14TL and 2YT (r = 0.181, P = 0.102).

The AUC for predicting fecal biomarker remission using 2YTL was 0.805 (0.695-0.914, P < 0.001) higher than W14TL: 0.694 (0.575-0.813, P = 0.004). 2YTL were independently associated with fecal biomarker remission: OR 1.321 (1.126-1.550), P = 0.001.

Patients with fecal biomarker remission were more likely to reach clinical remission (89.3% vs 55.6%, P = 0.001), persist with biologic therapy (92.9% vs 63.0%, P = 0.001) and present no negative outcomes (17.9% vs 59.3%, P < 0.001).

Conclusion: Proactive TDM induced fecal biomarker remission in a large percentage of patients which associated with better outcomes at 2-years. 2YTL correlated better than W14TL with target fecal calprotectin levels suggesting that pTDM improves treatment results.

Disclosure: Nothing to disclose

P0452

TO "D" OR NOT TO "D": IS INACCURATE TESTING CAUSING OUR VITAMIN D SUPPLEMENTATION TO BE OFF THE MARK? - LESSONS FROM INFLAMMATORY BOWEL DISEASE

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Introduction: Vitamin D deficiency is a common health issue across the globe, and especially prevalent in inflammatory bowel disease (IBD). Although it is not yet clear if the deficiency is a cause or a consequence of the disease, mounting evidence suggests that low vitamin D levels are associated with important clinical parameters and outcomes in patients with IBD, including disease activity, hospitalisation and surgery rates, health-care utilisation, effectiveness of biologic therapy, clinical relapse, and risk of bone loss. It is therefore critical to screen, diagnose and treat vitamin D deficiency in these patients. However, there are still doubts concerning the accuracy of routine vitamin D testing methods.

Aims & Methods: The aim of this study was to compare the clinical utility and outcomes of a commonly-used chemiluminescence immunoassay (CLIA) with the gold standard liquid chromatography-tandem mass spectrometry (LC-MS/MS) method in the detection of vitamin D deficiency/insufficiency in patients with IBD. This study was conducted as a prospective, cross-sectional study in adults with IBD. Full blood count, calprotectin and CRP were determined by routine assays. Serum 25-hydroxyvitamin D (25(OH)D) levels were determined by two different methods, a chemiluminescent immunoassay (CLIA), the method routinely used in the clinic,

and LC-MS/MS (Immundiagnostik, Germany) for comparison. CRP levels $\geq 5\text{mg/dL}$ and/or faecal calprotectin $\geq 200\text{ }\mu\text{g/g}$ were considered evidence of inflammatory activity. Vitamin D status of the participants was defined as follows: sufficiency, 30–100 ng/mL; insufficiency, 20–29 ng/mL; and deficiency, $< 20\text{ ng/mL}$. Statistical analysis was performed using IBM SPSS version 25.0.

Results: 188 patients with IBD (94 male, 94 female; 116 Crohn's disease (CD), 72 ulcerative colitis (UC); 109/188 with inflammation) aged 42.1 ± 13.0 years were recruited to the study. The correlation between 25(OH)D levels determined by the two tests was moderate ($r=0.533$, $p<0.001$). Limits of agreement analysis (LoA) showed a strong significant difference between the two methods' measurements of 25(OH)D levels ($p=0.002$). Compared to the LC-MS/MS method, the CLIA assay demonstrated a mean relative bias of 53.8% (min 0.0% - max 500.4%). Comparison with the LC-MS/MS results showed that the CLIA test failed to accurately diagnose vitD status in 28.2% of vitD-sufficient, 67.3% of vitD-insufficient and 50.9% of vitD-deficient patients ($p<0.001$).

Conclusion: Our comparison of CLIA versus the gold-standard LC-MS/MS methodology indicates that, despite its widespread use, CLIA methodology may mispredict 25(OH)D levels. Furthermore, the results do not present a predictable pattern/tendency for overestimation or underestimation of values. This may lead not only to wasted resources and oversupplementation in patients treated unnecessarily, but also to some patients being denied vital supplementation. While the clinical implications of these results require comprehensive evaluation and discussion, the question arises as to how vitamin D deficiency can be appropriately treated if we cannot rely on the diagnosis, as our data suggest.

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P0453

ULTRASONOGRAPHY TIGHT CONTROL AND MONITORING IN CROHN'S DISEASE DURING DIFFERENT BIOLOGICAL THERAPIES: A MULTICENTER STUDY

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Introduction: Bowel Ultrasonography (BUS) is a non-invasive tool for evaluating bowel damage in Crohn's disease (CD) patients (pts).

Aims & Methods: We report results from a multicenter study aimed at assessing changes in BUS parameters, including transmural healing (TH) induced by different biological therapies. We performed a prospective study at 16 sites in Italy, from February 2018 to February 2019 and followed for one year.

Our study included adult pts with CD and indication for biological treatment. Key BUS endpoints assessed at 3, 6 and 12 months were: bowel wall thickness (BWT), lesion length, echopattern, blood flow changes from baseline and BUS TH (normalization of all BUS parameters). The most affected bowel segment at baseline was used for all BUS parameters. Changes in BUS parameters after 3, 6 and 12 months were analyzed using Wilcoxon test and paired t test; difference between proportion and NNT was tested by Chi-square test. Logistic regression analyses were performed to find any determinant of risk for TH.

Results: One hundred and eighty-eight out of 201 CD pts were enrolled and analyzed (116 males [62%]; median age, 36 years; range 18–71; median disease duration, 72 months; range 3–636). Forty-seven per cent of pts had L1, 5% had L2, 46% had L3 and 1% others according to the Montreal criteria. Fifty-five per cent of pts were treated with adalimumab, 16% with infliximab, 13% with vedolizumab and 16% with ustekinumab. Indication for therapy was active luminal disease in 86% and steroid-dependence in 14%. Overall BUS TH rates at 12 months was 27.5% (Table 1) with a NNT of 3.6. TH at 12 months after adalimumab was 26.8%, 37% after infliximab, 27.2% after vedolizumab and 20% after ustekinumab. No statistically significant difference in speed of effectiveness of TH among therapies was observed. Mean BWT improvement from baseline was statistically signifi-

cant at 3, 6 and 12 months ($p < 0.0001$). Lesion length, ileal echopattern and blood flow improvements after 12 months of therapy were statistically significant ($p \leq 0.001$, $p = 0.001$, $p \leq 0.001$, respectively). Fissures, lymph nodes and fibrofatty proliferation after 12 months of therapy were statistically decreased ($p = 0.01$, $p < 0.0001$, $p < 0.0001$, respectively). Median Harvey-Bradshaw index, C-reactive protein and fecal calprotectin decreased after 12 months from baseline ($p < 0.0001$). Logistic regression analysis showed a greater BWT at baseline was associated with a lower risk of TH at 3 months [$p = 0.03$ (OR 0.70, 95%CI 0.50-0.97)] and 12 months [$p = 0.01$ (OR 0.58, 95%CI 0.38-0.89)].

BUS parameters	V0 Baseline n=188	V1 3 mos n=188	V2 6 mos n=171	V3 12 mos n=156	P value V1 vs. Baseline	P value V2 vs. Baseline	P value V3 vs. Baseline
Patients with normalization of lesion	-- --	31/188	42/171	43/156	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$
- Total patient - Ileal disease - Colon disease		23/158 8/30	32/146 10/25	32/133 11/23	NNT 6.1 (4.6-9.8)	NNT 4.1 (3.2-5.8)	NNT 3.6 (2.9-5.1)
BWT Median, range (mm) - Ileal disease - Colon disease	6 (3.4-11.5) 6.35 (4.3-9)	5.5 (3-10) 5.5 (4-8)	5 (3-10) 4.9 (4-8)	5 (3-9) 4 (4-8)	$p < 0.0001$ $p = 0.07$	$p < 0.0001$ $p = 0.01$	$p < 0.0001$ $p = 0.0004$
Lesion length (cm) - Ileal disease - Colon disease	15 (4-60) 40 (20-100)	10 (0-60) 30 (0-100)	10 (0-60) 20 (0-100)	10 (0-50) 0 (0-100)	$p = 0.009$ $p = 0.98$	$p = 0.0008$ $p = 0.0015$	$p < 0.0001$ $p = 0.004$
Echo pattern - Ileal disease - Preserved - Not preserved - Colon disease - Preserved - Not preserved	105 53 23 7	122 36 24 6	118 28 19 6	110 23 19 4	$p = 0.033$ $p = 0.7$	$p = 0.0046$ $p = 0.7$	$p = 0.017$ $p = 0.7$
Blood flow (Limberg score) - Ileal disease - 1 • 2 • 3 • 4 - Colon disease - 1 • 2 • 3 • 4	33 59 39 27 8 11 4 7	69 49 31 9 16 8 4 2	79 42 11 14 15 7 3 0	81 27 18 7 14 6 3 0	$p < 0.0001$ $p = 0.0056$	$p < 0.0001$ $p = 0.0017$	$p < 0.0001$ $p = 0.015$
Presence of stenosis with prestenotic dilatation - Ileal disease - Colon disease	13 0	11 0	13 0	12 1	$p = 0.6$	$p = 0.8$	$p = 0.2$
Presence of fissures - Ileal disease - Colon disease	16 1	11 1	11 1	4 0	$p = 0.3$	$p = 0.5$	$p = 0.012$
Presence of fistula - Ileal disease - Colon disease	2 0	2 0	5 0	4 0	$p > 0.99$	$p = 0.2$	$p = 0.3$
Presence of abscess - Ileal disease - Colon disease	0 0	0 0	1 0	0 0	$p > 0.99$	$p = 0.3$	$p > 0.99$
Presence of lymph node - Ileal disease - Colon disease	80 11	58 8	43 9	33 5	$p = 0.009$	$p = 0.0005$	$p < 0.0001$
Presence of fibrofatty proliferation - Ileal disease - Colon disease	94 15	64 9	57 6	44 6	$p = 0.0002$	$p < 0.0001$	$p < 0.0001$

[Table 1]

Conclusion: BUS TH was detected in about a quarter of CD pts after 12 months after biological therapies. This is the first multicenter study using BUS after different therapies for tight control and monitoring transmural bowel changes in CD.

Disclosure: Nothing to disclose

P0454

INTESTINAL ULTRASOUND IN MONITORING POSTOPERATIVE CROHN'S DISEASE

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Introduction: Complete ileocolonoscopy is the gold standard for the postoperative recurrence in Crohn's disease. Intestinal ultrasound (IUS) is a non-invasive, cost-effective method, but the current study situation with regard to the gold standard is not yet sufficient.

Aims & Methods: Retrospective data for postoperative monitoring were reviewed in three German IBD centers. Inclusion criteria: Crohn's disease, ileocecal resection or anastomosis revision, absence of a protective stoma. Furthermore, intestinal sonography and an ileocolonoscopy was performed. For intestinal sonography a wall thickness of more than 3mm in the neoterminal ileum was considered as a criterion for recurrence. For the ileocolonoscopy the Rutgeerts Score was used.

Results: A total of 329 patients were identified. In 228 cases at least one sonography or colonoscopy was performed within two years postoperatively. In 101 patients no sufficient data were available concerning postoperative follow-up. Of the 228 patients who were followed postoperatively ileocolonoscopy was performed in 111 (49.1%) cases within a period of 6 months and in 58 (25.4%) cases after 12 months post-op. In 145 cases, both sonography and ileocolonoscopy were performed at one of the four periods considered. The specificity of sonography for the detection of severe terminal ileitis, defined as Rutgeerts ≥ 2 , was 82.6% and the sensitivity 83.3%. Considering all cases of colonoscopically confirmed recurrence, i.e. Rutgeerts > 0 , the specificity of the sonography increased to 90.2%, while the sensitivity decreased to 64.9%.

Conclusion: Postoperative ileocolonoscopy is applied according to the guidelines in the majority of patients. The sensitivity and specificity of sonography are in agreement with previously published results in their investigations, which, however, examined a much smaller number of patients. For final clarification, a prospective study with a larger number of cases is needed.

Disclosure: UH has received a Lecture/Advisory board honorarium from MSD; AbbVie, Falk Foundation, Takeda, Mundipharma, Hospira, Ferring, Vifor, Mylan, Janssen, Pfizer, Celltrion

P0455

AGE RELATED PREVALENCE OF SEXUAL AND ERECTILE DYSFUNCTION AND LOW QUALITY OF LIVE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory Bowel Disease (IBD) has a negative impact on quality of life (QOL), and sexuality is one of its major determinants. The impact of disease characteristics on sexuality and intimacy is one of the main concerns of IBD patients. Despite the obvious relevance of this problem, knowledge of the extent of sexual dysfunction in persons with IBD is limited. **Aims & Methods:** The aim of the study was to determine the age related prevalence of sexual and erectile dysfunction and low QOL in patients with IBD and their predictors.

In this cross-sectional study patients fulfilled anonymous validated questionnaire on their sexual function. In International Index of Erectile Function (IIEF) for males, five domains were evaluated through questions on erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. In women were six domains assessed, desire, arousal, lubrication, orgasmic function, satisfaction and pain. For both scores, higher scores indicated a better function. Patients also fulfilled IBDQ-32, a validated questionnaire for assessing quality of life in IBD patients that consists of four main components (social, emotional, systemic and bowel function).

Results: We have analyzed 202 patients (122 male, 80 female), out of which there was 133 (65.8%) of CD patients. Average was 37 (29-47) years with disease duration of 10.93(4-16) years. Total IBDQ in males and females was 187.5 (157-205) and 178.5(153-195.5), respectively ($p < 0.05$). Prevalence of SD in men was 18% (22/122), that of ED 30.3% (37/122) and SD in women, 75% (60/80) ($p < 0.05$). In male patients SD and ED were highest among patients 21-30 years old (SD 23.5% and ED 38.2%) and again raising from 51 years and more. In female patients SD was constantly being highly prevalent, showing no decline over time, comparing group from 21-30 years and 31-40 years of age (60% vs 77.4%) (Table 1). Proportion of low QOL was similar in both gender groups (31.1% of male and 40%) of female patients ($p=0.253$). In both male and female patients, highest proportion of low QOL was in 51-60 years old group (58.3% in female and 50% in male patients), following 41-50 years old group. Overall, female patients had lower QOL thorough all age-related groups (Table 1). In multivariate analysis, significant predictors of SD in men were CD phenotype, disease duration and emotional domain of IBDQ, and of ED depression, emotional and bowel domain of IBDQ. Significant predictors of SD in women in multivariate analysis was emotional IBDQ domain.

Conclusion: Female IBD patients have constantly high SD prevalence, being higher after 30 years of age. In contrast, male patients have highest prevalence of SD and ED in age group 21-30 years old and further declining. Regarding age-related QOL, in contrast to SD, there is low QOL in both genders after 40 years of age. This could mean that in different age groups there is different perception on QOL. We hypothesize that different age-related groups could have different predictors or partly different pathophysiology of SD, ED and QOL which should be further investigated on larger sample.

Disclosure: Nothing to disclose

P0456

THE INCIDENCE AND CHARACTERISTICS OF VENOUS THROMBOEMBOLISMS IN PAEDIATRIC-ONSET INFLAMMATORY BOWEL DISEASE

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Introduction: Venous thromboembolism (VTE) is a rare event in children, with reported incidences ranging from 0.07 to 0.49 per 10,000 children in population based cohort studies. In hospitalized children the incidence may be increased up to 58 per 10,000 admissions. The risk of developing VTE is increased 2-fold to 3-fold in adults with inflammatory bowel disease (IBD) and is associated with disease activity, disease extent and IBD-related therapy. Studies in paediatric IBD patients suggest an increased risk of VTE as well, however exact incidence and risk factors are yet unknown. Clear guidelines on how to predict and prevent these complications in children are therefore lacking.

Due to the rarity of these events, international studies are needed to gain information on risk factors for this complication and optimize guidelines. With this study, we aim to assess the incidence and associated risk factors of VTEs in children with IBD.

Aims & Methods: As part of an international prospective safety registry, paediatric gastroenterologists reply monthly to an electronic survey to indicate whether they have encountered any of 10 predetermined complications, including VTE, in IBD patients < 19 years of age. Respondents of VTE were requested to fill out additional information on both the IBD and VTE. In addition, participating physicians annually report the number of new and current PIBD patients under their care, which combined with the reporting period, is the denominator data for this project.

Results: Since October 2016, over 150 paediatric gastroenterologists from 26 different countries have been participating in the safety registry. In total 18 cases of VTE were reported for 28,793 patient-years of follow up, resulting in an observed incidence of 4.86 per 10,000 PIBD patients annually (95% CI 2.66-8.16). This is at least a 10-fold increase compared to the VTE incidence in the general paediatric population.

Among cases with available additional information ($n=11$; 6 female, 5 male), were 4 cases of central venous sinus thrombosis, 4 upper or lower limb VTEs, 1 intra-cardiac thromboembolism and 1 pulmonary embolism. Of all children with VTE 7/11 had ulcerative colitis or IBD unclassified, of which five had pancolitis. 72% (8/11) of cases occurred during a disease flare, but only 45% during hospitalization.

None of the patients had received antithrombotic prophylaxis before the event occurred. No hereditary or acquired thrombophilia was detected in any of the cases. Physicians reported steroid therapy ($n=5$), immobility ($n=1$), trauma ($n=1$), total parenteral nutrition ($n=1$), surgery ($n=1$) and presence of a central venous catheter ($n=2$) as risk factors. Four thromboembolic events were life threatening, two resulted in significant disability and one resulted in death.

Conclusion: These data suggest a 10-fold increase of the VTE incidence in the paediatric IBD population compared to the general paediatric population. Most VTEs are reported in UC/IBD-U patients and occurred during an exacerbation of IBD, although not all are inpatients at the time. Ongoing

data collection will help to understand possible causes, gain insight into differences in management and outcomes of these complications and support the development of evidence-based guidelines.

Disclosure: Nothing to disclose

P0457

HISTOLOGICAL ACTIVITY SCORE IN CROHN'S DISEASE: A REAL LIFE 1-YEAR PROSPECTIVE STUDY

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Introduction: The role of histological degree of inflammation in Crohn's Disease (CD) in terms of relationship with clinical and endoscopic activity scores, also as a predictive marker of clinical relapse, is debated.

Aims & Methods: In a prospective study, we aimed to assess the correlation between clinical, endoscopic and histological activity scores. Secondary aim was to assess the role of histological activity as a predictor of clinical relapse within 1 year in a cohort of CD patients undergoing colonoscopy. From February 2016 to February 2017, consecutive CD patients undergoing colonoscopy according to clinical indications, were prospectively enrolled. Inclusion criteria were:

- 1) defined diagnosis of CD;
- 2) age ≥ 18 and < 80 years (yrs);
- 3) regular follow up (> 1 visit/yr);
- 4) complete colonoscopy;
- 5) indication for colonoscopy according to current European guidelines.

At colonoscopy, ≥ 2 biopsies were taken from ≥ 1 macroscopically involved areas. All colonoscopies were performed by the same IBD dedicated gastroenterologist. The day of colonoscopy, clinical activity was assessed with the Crohn's Disease Activity Index (CDAI) (activity ≥ 150) (1), endoscopic activity by the Simplified Endoscopic Score (SES-CD) (activity ≥ 3) (2). Histologic activity was assessed by the same IBD dedicated pathologist using the Global Histological Activity Score (GHAS) for CD (activity ≥ 4) (3). Scores were blindly assessed. Follow-up was planned at 1 yr. Data expressed as mean [range]; Pearson's index was used to investigate the association between clinical, endoscopic and histological activity, Student T-Test to assess differences between groups.

Results: The study cohort included 51 CD patients (M 30 [58.8%]; mean age 47.4 [19-75] yrs, CD duration 14 yrs [1-40] yrs). CD lesions involved the ileum in 28 (54.9), colon in 6 (11.8%), ileum-colon in 16 (31.4%), upper GI in 1 (1.9%) patient. CD behavior was non-stricturing non-penetrating in 16 (31.4%), stricturing in 21 (41.2%), penetrating in 14 (27.4%) patients; history of perianal disease was recorded in 16 (31.4%), surgery for CD in 26 (50.9%). The day of colonoscopy CD was clinically active in 7 (13.7%) patients, inactive in 44 (86.3%). Endoscopic activity was observed in 37 (72.5%) patients and microscopic activity (GHAS ≥ 4) in 6 (11.6%). A learning phase with initial intraindividual variations in terms of histological scores was required by the dedicated pathologist before assessing the tested biopsies. No correlation was observed between clinical vs endoscopic scores ($R=0.24$; $p=0.08$); clinical vs histological scores ($R=0.14$; $p=0.31$), endoscopic vs histological scores ($R=0.22$; $p=0.11$).

No significant differences were detected in terms of median histological activity score between endoscopically active vs inactive patients ($p=0.07$). Clinical relapse occurred within 1 yr in 16 out of 51 (31.4%) patients. When

considering the 16 patients developing clinical relapse within 1 yr, at baseline clinical activity was observed in 5 (31.3%), endoscopic activity in all the 16 (100%) patients and histological activity in 4 (25%) patients.

Conclusion: In our cohort of patients, no correlation was observed between clinical, endoscopic and histological activity. All patients showing endoscopic activity at baseline experience a CD clinical relapse within 1 yr of follow-up, while clinical and histological activity at baseline appeared not to predict relapse.

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Disclosure: Nothing to disclose

P0458

EXPLORING HYPOPHOSPHATAEMIA: HOW FREQUENTLY DOES IT OCCUR IN INFLAMMATORY BOWEL DISEASE AND WHAT ARE THE IMPLICATIONS FOR INTRAVENOUS IRON THERAPY?

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Introduction: Hypophosphataemia (HP) is uncommon in the general population and mostly an incidental finding. However, it is under discussion as a common adverse effect of intravenous (IV) iron therapy in patients with inflammatory bowel disease (IBD). Since IV iron therapy is recommended as first-line therapy in many situations in IBD, it is important to define the frequency and possible causes of pre-existing HP.

Aims & Methods: The aim of this study was to investigate the occurrence of hypophosphataemia in patients with IBD, independent of IV iron therapy. This study was conducted as a comparative, cross-sectional study in adults with IBD ($n=190$) and healthy controls ($n=82$). Blood count, transferrin, albumin, phosphate, calprotectin and CRP were determined by routine assays. 25(OH)D levels were determined by ELISA. CRP levels ≥ 5 mg/dL and/or faecal calprotectin ≥ 200 μ g/g were considered evidence of inflammatory activity. Mild, moderate and severe HP were defined as a serum phosphate level of 2.0- $<$ 2.5 mg/dL (mild decrease), 1- $<$ 2.0 mg/dL (moderate), and $<$ 1 mg/dL (severe), the normal reference range being 2.5- $<$ 4.5 mg/dL. Statistical analysis was performed using IBM SPSS version 25.0.

Results: 190 subjects with IBD (95 male, 95 female; 122 Crohn's disease (CD), 68 ulcerative colitis (UC); 67/190 with inflammation) aged 41.7 $\pm$ 13.2 years in mean, and 82 controls (31 male, 51 female), mean age 50.5 $\pm$ 13.7 years, were recruited to the study. In the IBD patient group, 11.1% were found to have HP, in 23.8% of cases moderate and in 76.2% mild. In the control group, 9.8% were found to have HP (25% moderate, 75% mild). Thus, the frequency of hypophosphataemia was not found to differ between IBD patients and controls ($p=0.751$). None of the patients with IBD and no controls had severe hypophosphataemia. HP was more common in CD (12.3%) versus UC (8.8%), slightly more common in vitamin D-deficient patients (18.4%) compared to patients without vitamin D deficiency (11.2%), and similar in iron deficient/anaemic (9.8%) versus non-iron deficient patients (10.1%). Only the inflammatory status of the patients with IBD was found to have an effect on serum phosphate levels: The frequency of HP was 14.9% and 9.0% in patients with versus without inflammation, respectively ($p=0.041$). Additionally, CRP values showed a negative weak but significant correlation with phosphate values ($r=-0.252$, $p=0.013$).

Conclusion: HP was found to be more common in patients with IBD compared with controls, and more common in CD than UC. The prevalence of HP was increased in the presence of inflammation and/or vitamin D deficiency. In a clinical setting, therefore, serum phosphate levels should be assessed in patients with IBD - especially those with active inflammation and/or vitamin D deficiency - before considering IV iron therapy, in order to prevent severe HP.

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P0459

ENDOSCOPIC AND HISTOLOGIC ACTIVITY ASSESSMENT CONSIDERING DISEASE EXTENT AND PREDICTION OF TREATMENT FAILURE IN ULCERATIVE COLITIS

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Introduction: DUBLIN score allows evaluation of disease activity and extent in Ulcerative Colitis (UC).

Aims & Methods: This study aimed to evaluate DUBLIN score as a predictor of therapeutic failure and clinical remission as well as to associate endoscopic and histological activity scores to assess their joint performance. Retrospective cohort study, with consecutive inclusion of patients undergoing total colonoscopy with serial biopsies between 2016-2019. DUBLIN score (0-9) was calculated as the product of Mayo endoscopic score (0-3) by disease extent (E1-E3). Histological activity was evaluated through Nancy score (0-4). Activity scores were correlated with biomarkers, treatment failure (therapeutic escalation, hospitalization and/or colectomy) and clinical remission at 6-months (Mayo partial score < 2).

Results: One-hundred and seven patients were included. In 38.3% (n=41) there was evidence of endoscopic activity (Mayo ≥ 2) and in 50.5% (n=54) histological activity (Nancy ≥ 2). Mayo and DUBLIN scores showed good correlation (r=0.943; p < 0.001) and both were significantly higher in patients with histological activity (p < 0.001).

Therapeutic failure occurred in 25.2% (n=27). Mayo, DUBLIN, and Nancy scores were significantly associated with therapeutic failure (p < 0.001). The areas under the (AUC) ROC curve were 0.74 (Mayo; p < 0.001), 0.78 (DUBLIN; p < 0.001) and 0.84 (Nancy; p < 0.001). Joint evaluation of endoscopic and histological activity by combining DUBLIN and Nancy scores was associated with therapeutic failure with a significantly higher AUC of 0.84 (p < 0.001) compared to the Dublin score alone (p=0.003).

Conclusion: Mayo and DUBLIN endoscopic scores correlated with each other and with histological activity. The joint evaluation of endoscopic and histological activity allowed to predict with greater accuracy treatment failure.

Disclosure: Nothing to disclose

P0460

IN CONTRAST TO FAECAL CALPROTECTIN (FC), INCREASED FAECAL ALPHA-1-ANTITRYPSIN (A1AT) EXCRETION IS ASSOCIATED WITH LOW THROUGH LEVELS IN PATIENTS WITH SEVERE ULCERATIVE COLITIS LACKING RESPONSE TO MONOCLONAL ANTIBODY (MAB) THERAPY

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Introduction: The impact of gastrointestinal immunoglobulin leakage on therapeutic pharmacokinetic of mAb has been suggested by several clinical studies that demonstrated that the clearance of several therapeutic mAb is higher in patients with diseases known to cause intestinal protein loss. Most recently by measuring faecal Infliximab (IFX) concentrations, it has also been shown that in patients with moderate to severe ulcerative colitis (UC) intestinal loss of Infliximab was associated with a high rate of treatment failure (1).

However, due measuring faecal mAb concentration in a routine setting is cumbersome and costly. Because faecal A1AT has been widely used as a diagnostic biomarker for to evaluate intestinal protein leakage, we hypothesized that increased faecal A1AT should be a useful diagnostic tool predicting increased mAb clearance from a "leaky gut".

Aims & Methods: Up to April 2020 we collected faecal samples from 50 consecutive patients with mAb (infliximab, adalimumab, vedolizumab, ustekinumab) with moderate to severely active UC during the first 6 weeks of mAb therapy at the iCCC. Serum mAb trough levels, faecal calprotectin and A1AT concentrations were measured using enzyme-linked immunosorbent assays (Immundiagnostik AG, Bensheim, Germany). Clinical and endoscopic responses were assessed 6 and 12 weeks after treatment began.

Results: Patients that were clinical nonresponders at week 6 had significantly higher faecal concentrations of A1AT and insufficient mAb trough levels at baseline and week 6 than patients with clinical responses (median concentration > 1760 µg/g in nonresponders vs 240 µg/mL in responders; p = 0.0047). There was no correlation for faecal calprotectin and we did not observe a correlation between faecal calprotectin and A1AT.

Conclusion: Intestinal loss of mAb in moderate to severely active UC is associated with a diminished response to mAb treatment. Patients with severe disease, therefore, will benefit from more intensive dosing regimens. We report here for the first time that in patients with moderate to severely UC intestinal loss of A1AT is associated with treatment failure of mAb, independently of the class of mAb used. Clinical studies, including population PK studies assessing faecal A1AT are warranted to further validate our findings and, possibly, to allow improved prediction of mAb pharmacokinetics in patients with diseases known to cause intestinal protein loss.

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P0461 WITHDRAWN

P0462

BODY COMPOSITION ANALYSIS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Childhood inflammatory bowel disease (IBD) is associated with weight loss and growth failure. Malnutrition may be the result of reduced oral intake, increased nutrient requirements, gastrointestinal losses of nutrients, and sometimes from drug action in IBD. These deficiencies can lead to a change in body composition.

Aims & Methods: The aim of our research is to define the body composition alterations in children with IBD and explore the effects of disease stage. We assessed anthropometry and body composition in 33 children (14 girls and 19 boys) aged 6-17 years with IBD. 28 (84%) patients have ulcerative colitis (UC), of which 3 are children in the onset of the disease, 13 patients are in remission, and 12 children are relapsed. 5 (15%) have Crohn's disease (CD) in remission. The WHO AnthroPlus program and bio-electrical impedance analysis (BIA) were used to assess the parameters of the nutritional status.

Results: Nutritional status disorders were detected in half of children with IBD. In 4/12 children (33%) and 3/12 children (25%) with UC in relapse were diagnosed mild to moderate malnutrition, respectively. Severe malnutrition was detected only in 1 patient in the same stage (8%). Regarding the onset of the UC, two-third of all children had moderate malnutrition. BIA data showed a deficiency of lean mass (LM) and active cell mass (ACM) in 7 children (58%), a more frequent excess of fat mass (FM) in 5 children (41%) than its deficiency (16%). Also a decrease of the phase angle (PA) $< 5.40^\circ$ and $< 4.40^\circ$ was recorded in 3 patients (25%) and 2 patients (16%), respectively.

As for the UC in remission, malnutrition was detected only in 3/13 of children (23%). According to BIA in 5 children (38%) was remained LM and ACM deficiency. Increase of FM was revealed in 5 children (38%) and decrease of FM - only in 1 child (7%). The low PA ($< 5.4^\circ$) was recorded in 3 children (23%), there were no children with value of PA $< 4.4^\circ$ in inactive UC. With regard to children with Crohn's disease in remission, there were detected a moderate malnutrition in 3 children (60%). According to BIA there were revealed a LM and ACM deficiency. FM was normal and PA values were $< 5.4^\circ$ in the most of children with inactive Crohn's disease.

Conclusion: According to our preliminary data, nutritional status disorders were identified in most children with IBD, mainly due to malnutrition, which manifest themselves not only in a lack of body weight and growth retardation, but also in changes in body composition. The frequency of the body component composition alteration depends on the stage of the disease.

Despite the ongoing treatment, nutritional status abnormalities persist during remission of IBD - especially in Crohn's disease. To understand what impact this may have on health and disease in children with IBD, further studies are needed.

Disclosure: Nothing to disclose

P0463

VENOUS THROMBOEMBOLISM AFTER RECENT INFLAMMATORY BOWEL DISEASE FLARE: OUTCOMES AND PREDICTORS

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Introduction: Venous thromboembolism (VTE) poses increased morbidity and mortality in patients with inflammatory bowel disease (IBD). There is limited evidence on specific readmission rates for VTEs in IBD patients who have been recently discharged from the hospital due to an IBD flare. We aim to study post-IBD flare incidence, outcomes and predictors for VTEs.

Aims & Methods: Large cohort study of the 2016 National Readmission Database (NRD) of adult patients readmitted for VTE after an index admission of IBD flare. ICD-10CM/PCS codes were used to identify patients with IBD, VTE, other comorbidities and procedure. Primary outcome was specific readmission rate for VTE within 90-days of discharge. Secondary outcome was hospital economic burden. Independent risk factors for readmission were identified using Cox regression analysis.

Results: A total of 50,799 patients had a primary discharge diagnosis of IBD flare, out of which 0.3% (n= 165) had a 90-day specific readmission specifically for VTE. Patients readmitted with VTE are more likely to be obese (14.5% vs. 7.9%; $P=0.04$), have diabetes type 2 (20.1% vs. 8.9%; $P<0.01$), to have higher rate of central parenteral nutrition (4.7% vs. 1.7% $P=0.03$), to have prior history of pulmonary embolism (12.5% vs. 0.3% $P<0.01$), prior DVT (36.8% vs. 0.4%; $P<0.01$), to have higher Charlson comorbidity score ≥ 3 (19.5% vs. 6.7%; $P<0.01$), to have Medicare as primary payer (40.6 vs. 27.1%; $P=0.05$). A total of 834 days were associated with readmission and the total health care in-hospital economic burden of readmission was \$6,755,985 (in charges) and \$1,849,146 (in costs). Independent predictors of readmission were older age (aOR 1.02; $P=0.04$), having peripheral parenteral nutrition during the index admission (aOR 3.65; $P=0.03$), undergoing colonoscopy with or without intervention during the index admission (aOR 3.95; $P<0.01$), and having Medicaid as primary payer during the index admission (aOR 2.49; $P=0.01$).

Conclusion: The rates of VTE after a recent IBD flare that required hospitalization was 0.3% and this could be due to the inflammatory state that an IBD flare poses. However, providers that take care of hospitalized IBD patients should be aware of these findings and provide appropriate VTE prophylaxis during the hospitalization to help decrease post-discharge VTE rates. Finally, VTEs poses a high economic health care burden in IBD patients and there are specific risk factors that can be targeted to help reduce the risk for readmissions.

Disclosure: Nothing to disclose

P0464

ACUTE SEVERE ULCERATIVE COLITIS: IS THE NEW SCORE PROPOSED BY ACG BETTER TO PREDICT TREATMENT OUTCOMES?

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Introduction: Up to 33% of patients admitted by acute severe ulcerative colitis (ASUC) show no response to intravenous corticosteroids (IVC), needing rescue therapy (medical and/or surgery). Recently, the American College of Gastroenterology (ACG) proposed, in its guidelines, a new score to assess the severity of UC; however, this score has not yet been validated, in particular in the subset of patients with ASUC.

Aims & Methods:

Aims: Assess the accuracy of the score proposed by the ACG in determining the course of disease and the response to therapy in patients with ASUC admitted in hospital, comparing with other scores routinely used.

Methods: All consecutive patients admitted to our tertiary referral center due to ASUC, between January 2010 and January 2020, were enrolled in this retrospective study. ASUC was defined according to the adapted True-love and Witts criteria and all patients were treated with IVC. Main outcomes evaluated were failure of IVC treatment, need for rescue medical therapy (RMT) (infliximab and/or cyclosporine) and/or colectomy. For all admissions the following severity scores were calculated: Proposed ACG Ulcerativ Colitis Activity Index (pACGUCI), MES (Mayo Endoscopic Score), SCCAI (Simple Clinical Colitis Activity Index), Mayo Score (MS), Oxford Score (OS), Lindgren Score (LS) and Edimburg Score (ES). Each score accuracy to predict outcomes was calculated and compared between them.

Results: We included 281 hospital admissions (165 patients), 54% males, with a mean age of 40±17 years. The IVC failure was 32%, the needed of RMT 31% and TC 3.6%. Fulminant colitis as classified in the pACGUCI was associated with IVC failure (63.6% vs 28.2%, $p < 0.001$) as well as need for RMT (57.6 vs 27%, $p < 0.001$). In multivariate analysis, C-reactive protein >10 mg/L in the 3rd day of IVC, [OR=4.019(1.884-8.573), $p < 0.001$], LS >8points [OR 9.686(1.258-74.557), $p=0.029$] and MS >10points [OR 7.922(1.091-57.515), $p=0.041$] were independent predictors of IVC failure. Regarding comparison with other scores, the pACGUCI showed inferiority to predict IVC failure compared to LS and ES [AUC 0.619 (0.544-0.694), $p=0.003$ vs AUC 0.671(0.595-0.747), $p < 0.001$ vs AUC 0.622 (0.543-0.700), $p=0.002$, respectively] but superiority compared to MS [AUC 0.606(0.533-0.680), $p=0.007$], MES [AUC 0.590(0.516-0.664), $p=0.022$], OS [AUC 0.573(0.495-0.652), $p=0.063$], SCCAI [AUC 0.570(0.494-0.646)] and UCEIS [AUC 0.564(0.486-0.642), $p=0.040$]. Regarding the prediction of RMT, all scores behaved similarly, with an AUC 0.613 (0.537-0.689), $p=0.039$ for the pACGUCI. In relation to colectomy, only one score (UCEIS>7 at admission) presented a discriminant ability higher than the other scores [AUC 0.700(0.518-0.881), $p=0.033$].

Conclusion: Despite its ability to identify cases of IVC failure and the need of RMT, the pACGUCI does not have a discriminating ability higher than other scores already used. Prospective studies will be necessary to confirm the results obtained.

Disclosure: Nothing to disclose

P0465

DUBLIN SCORE: AN ENDOSCOPIC SCORE TO QUANTIFY INFLAMMATORY ACTIVITY IN ULCERATIVE COLITIS

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Introduction: Inflammatory activity during Ulcerative Colitis (UC) can be estimated using clinical, biological and endoscopic criteria.

The DUBLIN score is an endoscopic score used to assess the inflammatory burden of the UC by combining the severity and the extent of the disease.

Aims & Methods: The aim of this study is to evaluate the clinical utility of this score by comparing its performance to other biomarkers of inflammation.

A retrospective study was conducted over UC patients which were hospitalized in the gastroenterology department A in RABTA hospital between January 2012 and September 2019. Clinical, biological and endoscopic features were abstracted from medical records. The DUBLIN score was calculated as a product of the Mayo Endoscopic Score [0-3] and disease extent based on Montreal classification [E1-E3]. (it varies between 0 and 9).

Results: A total of 72 patients were included in this study. The sex ratio was 0.6 and the mean age was 39 years (18-78 years). The average course of the disease was 25 years (0-25 years). The extent of the disease was evaluated as E2 in 41.7% of patients and E3 in 58.3% of them. The mean CRP level was 38.4 mg / dl (3-205 mg / dl). During the colonoscopy, the average of the Mayo endoscopic score was estimated at 2.33 (2-3) and that of the Dublin score at 6.14 (4-9). In order to treat the flare, salicylates were prescribed in 44.4% of patients, oral corticosteroid therapy in 26.4%, 33.3% of them needs an intravenous corticosteroid therapy and 5.6% needs ciclosporin. Colectomy was performed in 9.7% of patients. The DUBLIN score was significantly correlated with CRP ($p = 0.008$) and a high Dublin score is associated with a higher risk of colectomy ($p = 0.028$).

Conclusion: The DUBLIN score is a simple tool to assess the inflammatory burden of the disease during UC which may reflect the severity of the inflammation and the risk of colectomy.

Disclosure: Nothing to disclose

P0466

SYMPTOMATOLOGY AND QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE. IS THERE A GOOD CORRELATION BETWEEN THEM AND INFLAMMATORY ACTIVITY?

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Introduction: The symptomatology in inflammatory bowel disease (IBD) is very variable and sometimes its intensity is not well correlated with the inflammatory activity. Some patients suffer functional symptoms that complicate the assessment and management of IBD. All this symptomatology, not only related to inflammation but also functional, impact negatively in the perception of the quality of life by patients.

Aims & Methods: To study the association between IBD symptomatology, patient's perception of the quality of life and inflammatory activity measured by colonoscopy. Consecutive IBD patients referred for colonoscopy according to our center protocol, who complete colonic examinations and clinical surveys were recruited. The following questionnaires were performed: Harvey-Bradshaw index for Crohn disease (CD), partial Mayo score for Ulcerative Colitis (UC), and the Questionnaire of Quality of life (QQL) for all IBD patients. Positive and negative predictive values (PPV, NPV), sensitivity (Se), specificity (Sp), and area under ROC curve (AUROC) were calculated for each questionnaire.

Results: 103 patients (53.7% female, median age 52 years, IQR 42-61) were finally included. 52 (50.4%) with UC and 51 (49.6%) with CD. 23 (22.3%) patients reported clinical activity, 13 mild, 9 moderate, and 1 severe clinical activity. On the other hand, we detected endoscopic activity in 41 (39%) patients. Diagnostic accuracy for Harvey -Bradshaw index and partial Mayo score scores are summarized in Table 1.

	Se	Sp	NPV	PPV	AUROC
All IBD Patients	43.99%	91.9%	71.3%	78.3%	0.670
UC patients (Partial Mayo)	35.7%	94.6%	71.4%	79.5%	0.652
CD patients (Harvey-Bradshaw)	46.2%	88.8%	61.9%	80.0%	0.671

[Table 1. Diagnostic accuracy for Harvey -Bradshaw index and partial Mayo score scores.]

Within patients that reported clinical symptoms, 21,5% UC and 20% CD patients did not show endoscopic activity so that symptoms could be classify as functional. On the other hand there were 28,6% UC and 38,1% CD patients that did not report any symptom but had endoscopic activity. The results for the QQL showed an association between the quality of life perceived by patients, the presence of symptoms, and also the presence of endoscopic activity ($p < 0,05$). Patients without endoscopic activity had a median score of 73.6/100 while those with endoscopic activity had

69.05/100. On the other hand, patients that report clinical activity had a score of 62.3/100, and asymptomatic patients had 73.6/100. Given these results, it seems like the presence of symptomatology has more influence than the presence of endoscopic activity in the perceived quality of life by patients.

Conclusion: The presence of symptomatology in IBD patients is only partially related with inflammatory activity, existing patients that report functional symptoms. However, this kind of symptoms causes likewise a decreased perceived quality of life, so that its approach and treatment should be equally important in our clinical practice.

Disclosure: Nothing to disclose

P0467

PILLCAM CROHN'S CAPSULE - THE USE OF A PANENTERIC CAPSULE ENDOSCOPY IN A PORTUGUESE CENTER

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Introduction: In Crohn's disease (CD), the small bowel (SB) is affected in about 75% of the patients. PillCam Crohn's capsule (PCC) was recently introduced and is composed by two-headed cameras, allowing an extensive coverage of the entire gastrointestinal (GI) tract. Lewis score (LS) and Capsule Endoscopy Crohn's Disease Activity Index (CECDAl) are validated scores to evaluate SB activity. Recently the latter score was extended to the colon for standardization of inflammatory activity (CECDAlc) in PCC. For small-bowel CD, the endoscopic scores did not appear to correlate well with biomarkers and clinical activity, as it was already proved in our center. However, the evidence about this correlation for the entire GI tract evaluated by PCC is scarce.

Aims & Methods: Our aim is to correlate endoscopic activity in PCC with clinical (Harvey-Bradshaw index (HBI)) activity and biomarkers (fecal calprotectin, C-reactive protein (CRP)).

A retrospective analysis of PCC in patients with established CD was performed. The authors assessed indication; cleansing; LS, CECDAl and CECDAlc scores; HBI, CRP and fecal calprotectin close to PCC. Spearman Correlation was used to correlate each of the parameters (HBI, CRP and calprotectin) with PCC endoscopic activity scores. The authors considered a $p < 0.05$ to be statistically significant.

Results: 24 patients were included, 66.7% were female with median age of 39.9 years. The main indication for PCC was assessment of treatment response in 58.3%. All patients had an adequate enteric cleansing and 95.8% had an adequate colonic cleansing. 79.2% presented endoscopic activity, with 20.9% with only small bowel activity and 58.3% with panenteric activity. Median values obtained for LS were 900 [C1] (IQR 225-1004), CECDAl 9 (IQR 3-11.75), CECDAlc 11 (IQR 3.75-19.5), HBI 2 (IQR 0-3.75), CRP 0.39 (IQR 0.18-0.70) and calprotectin 295 (IQR 58.5-544). HBI correlated with all the endoscopic scores, with a moderate correlation with CECDAl ($rs=0.544$, $p=0.006$) and CECDAlc ($rs=0.627$, $p=0.001$), and with weak correlation with LS ($rs=0.465$, $p=0.022$). There was only a moderate correlation between CRP and CECDAlc ($rs=0.543$; $p=0.009$), but no correlation with LS or CECDAl correlated with CRP ($p>0.05$). Calprotectin did not correlate with any endoscopic score. No complications were reported.

Conclusion: This study concluded that HBI and CRP showed to be moderately correlated with CECDAlc. The small bowel endoscopic scores (LS and CECDAl) showed a weak to moderate correlation with clinical activity, evaluated by HBI. Moreover, there was no association between biomarkers and small bowel endoscopic scores. These results may suggest a better

correlation of symptoms and biomarkers in patients with involvement of the colon, and the importance of an endoscopic evaluation with capsule endoscopy in the management of patients with CD.

Disclosure: Nothing to disclose

P0468

COVID-19 OUTBREAK IMPACTING QUALITY OF LIFE AND SELF-PERCEIVED STRESS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is a chronic inflammatory disorder that not only has biological consequences, but also affects many other aspects of a patient's life and impairs their quality of life (QoL). The outbreak of COVID-19 has led to dramatic re-adjustment of social habits and health systems. This has generated uncertainty in patients with IBD, they wonder if they should stop their advanced therapies such as biologics, if they would have a worse outcome if they became infected and if they will have access to their treatments due to mobility restrictions. It is unknown what impact the COVID-19 outbreak and limitation of access to health services may have on IBD patients' QoL, as well as on their self-perceived stress.

Aims & Methods: To assess the influence of the COVID19 outbreak on the QoL and self-perceived stress of patients with clinically stable IBD receiving biological treatment.

We performed an observational study in IBD patients treated with biologics (anti-TNF, anti IL23/12 and anti integrin) at our outpatient IBD clinic for at least 6 months. To be included, patients had to be in stable clinical remission (Clinical activity index < 2 for Ulcerative colitis (UC) and Harvey-Bradshaw < 4 for Crohn's disease (CD) patients). We contacted patients telephonically and sent the questionnaires electronically. Patients filled the IBDQ9 questionnaire and the Perceived stress scale (PSS) at home. The IBDQ9 is a 9 item IBD-specific QoL questionnaire. Responses to each item are scored on a seven-point Likert scale in which 7 corresponds to the highest level of function and 1 to the lowest. The PSS is a 10 item questionnaire that measures the degree to which individuals appraise situations in their life as stressful. A higher score indicates a higher level of stress. We compared the results of the current IBDQ9 with the last IBDQ9 filled by the patient prior to the COVID19 outbreak to determine any changes. Clinical and demographic data were also collected.

Results: To date we have included 33 patients. Sixty-three percent were male, 12 had a UC diagnosis and 21 CD. Median age was 39 (33-44). Median baseline IBDQ9 was 58 (52.75-61.25) and last IBDQ9 (after COVID19 outbreak) was 53 (50-59.25). Related-samples wilcoxon signed rank test showed a significant difference between the IBDQ9 scores ($p < 0.05$). Median PSS was 12 (8.75-19.25). We determined spearman's correlation between the self-perceived stress questionnaire and the IBDQ9 and found a negative correlation with a $r = -0.63$ ($p < 0.01$).

Conclusion: QoL significantly decreased after the COVID19 outbreak in IBD patients in clinical remission treated with biologics. Higher self-perceived stress score was associated with a lower QoL

Disclosure: Nothing to disclose

P0469

COLORECTAL CANCER RISK IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH HIGH-GRADE DYSPLASIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Patients with inflammatory bowel disease (IBD) bear an increased risk to develop colorectal cancer (CRC). These cancers develop through an inflammation-dysplasia-carcinoma pathway. Especially patients with high-grade dysplasia (HGD) are at increased risk. However, the prognosis of HGD remains uncertain since aggregated data are based on studies from several decades ago(1). Moreover, endoscopic surveillance and treatment techniques improved in recent years. Therefore, we conducted a systematic review and meta-analysis to assess the prevalence and risk factors of CRC development in IBD patients with HGD.

Aims & Methods: We searched MEDLINE, EMBASE and the Cochrane Library to identify studies that reported rate and/or risk factors of CRC in IBD patients with HGD. Two researchers independently performed study selection, quality assessment with a modified QUIPS tool, and data extraction(2). Prevalence's and odds ratios (OR) were pooled with a random effects model. Furthermore, we applied explorative subgroup analyses. All included studies were subdivided into two separate groups given differences in study population and expected CRC risk. The first group, further referred to as 'surveillance cohort', consists of cohort studies including IBD patients undergoing regular endoscopic surveillance. The second group, further referred to as 'colectomy cohort' comprises of cohort studies in which all IBD patients underwent (procto-)colectomy. Subsequently, they retrospectively assessed the presence of colorectal neoplasia in prior colonoscopies and the colectomy specimen.

Results: We included nine 'surveillance cohort' studies ($n=452$ patients) and six 'colectomy cohort' studies ($n=358$ patients). The pooled prevalence of colorectal cancer in 'surveillance cohort' studies was 30.2%, with a pooled OR of 14.0 (95% CI 6.0-32.3) compared to the general cohort population. Duration of follow-up was described in three studies with a range between one and 15 years. 'Colectomy cohort' studies showed a pooled CRC prevalence of 32.2%, with a pooled OR of 7.7 (95% CI 2.7-21.4). Studies ≥ 1990 (all multicenter) reported a significantly lower risk for CRC compared to older, all monocenter studies (pooled OR 5.5 (95%-CI 2.9-10.7) vs 24.5 (95%-CI 7.8-76.4), $p=0.03$). In addition, studies with ≥ 20 HGD patients demonstrated a lower CRC risk compared to smaller studies, although not statistically significant (pooled OR 8.4 (95% CI 3.5-20.3) versus 29.6 (95% CI 4.9-178.6), $p=0.22$). Aggregated data showed multifocal lesions, concomitant primary sclerosing cholangitis (PSC) and non-polypoid lesions as risk factors for CRC after HGD.

Conclusion: The CRC risk in IBD patients with HGD remains high, with a CRC prevalence of approximately 30% following HGD. The CRC risk significantly declined in studies performed after 1990. Multifocal, non-polypoid lesions and PSC are reported to bear the highest risk of CRC development. These findings may aid optimization of risk stratification and treatment strategies in IBD patients with HGD.

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Disclosure: Nothing to disclose

P0470

DIAGNOSTIC AND PROGNOSTIC VALUES OF ANTI-GLYCOPROTEIN 2 ANTIBODIES (GP2A) IN INFLAMMATORY BOWEL DISEASES: RESULTS OF A RETROSPECTIVE MONOCENTRIC COHORT STUDY

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Introduction: We are always looking for tools that can help clinicians to better diagnose Inflammatory Bowel Diseases (IBD) and to anticipate their evolution. Anti-pancreatic antibodies, especially anti-glycoprotein 2 antibodies (GP2a) appear to be useful but their added value compared to usual antibodies (Anti-Saccharomyces Cerevisiae Antibodies (ASCA), Anti-Neutrophil Cytoplasmic Antibodies (ANCA)) remains unclear.

Aims & Methods: We performed a retrospective cohort study including 369 adults with Crohn's disease (CD) and 151 adults with ulcerative colitis (UC) in whom the detection of GP2a, ASCA and ANCA was performed at the Hospices Civils de Lyon between September 2013 and April 2019. We have determined a control group with 80 patients suffering from Irritable Bowel Syndrome (IBS) who had also a GP2a evaluation. GP2a and ASCA were identified in sera by dedicated Enzyme-Linked ImmunoSorbent Assays (ELISA), and ANCA were detected by indirect immunofluorescence in a blinded fashion.

Results: Significantly more IBD patients were positive for GP2a (IgA and/or IgG) compared to IBS patients (25.8% vs 12.5%, $p=0.007$). The prevalence of GP2a was higher in CD compared to UC patients (30.1% vs 15.2%, $p < 0.001$), whereas the difference was not significant between UC and IBS patients. GP2a sensitivity was far from ASCA sensitivity to diagnose IBD vs IBS (26.1% and 44.6%, respectively) or CD vs UC (30.6% and 55.8%, respectively), but GP2a specificity was slightly better (85% and 82.8%, respectively). We observed that 79% of CD patients who had GP2a were also positive for ASCA. In addition, 14% of ASCA-negative CD patients were positive for GP2a. In CD, the GP2a-associated disease outcomes were similar to those associated with ASCA (early onset of disease, ileal involvement, complicated behaviors, use of last-line biologics and need for surgery). However in ASCA-negative CD patients, the positivity of GP2a allowed to restore some disease outcomes associated in ASCA-positive patients (complicated behaviors, use of last-line biologics and need for surgery), but also was associated with an increased risk of CD-related perineal lesion, which was specific for this ASCA-negative / GP2a-positive subset of patients.

Conclusion: Our study confirmed the diagnostic and prognostic value of GP2a in CD but ASCA remain the most accurate serologic markers. GP2a assay might be useful as an additional non invasive diagnostic and prognostic tool in ASCA-negative CD patients.

Disclosure: Nothing to disclose

P0471

RISK FACTORS FOR POOR POSTOPERATIVE OUTCOME IN PATIENTS WITH CROHN'S DISEASE UNDERGOING ILEOCECAL RESECTION

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Introduction: Patients with inflammatory bowel diseases are at higher risk to develop postoperative complications. The objective of this study was to identify risk factors on 30-day postoperative outcome in patients who underwent ileocecal resection due to Crohn's disease (CD)

Aims & Methods: We have conducted a retrospective monocentric study including patients operated between January, 1st 2008 and september, 30th 2017. Epidemiologic, clinical, biologic and therapeutic characteristics were abstracted from medical records. Data entry and analysis were performed by SPSS version 23.0.

Results: We have colliged 89 patients of mean age of 32.79 years old. The indication for ileocecal resection was stricturing disease in 52 (57, 8%) cases and penetrating complications in 38 (42, 2%) cases.

Preoperative medical therapy included steroids ($n = 14$; 15,6%), immunosuppressants ($n = 13$; 14,4%), and biologics ($n = 4$; 4,4%). In 55 (61, 1%) patients, laparoscopic ileocecal resection was performed, while 34 (37, 8%) patients underwent an open ileocecal resection.

Post-operative complications had been observed for 7 patients (7, 8%), after a median time of 11,7 days (5-21), while 82 patients (91,1%) had an uneventful postoperative course. The rates of intra-abdominal abscess, anastomotic leak and enteric fistula were 4,4%, 1,1% and 2,2%, respectively.

Postoperative complications were associated with no blood transfusion ($p=0.016$) and a lower preoperative cholesterol level ($p=0.016$). Intra-abdominal abscess discovered during surgery ($p=0.018$) and laparotomy (71, 4% vs 36, 6%, $p=0.03$) were correlated with longer stay in hospital.

Other potential risk factors, such as age, gender, low preoperative haemoglobin or albumin levels, and the use of steroids or biologicals were not associated with the occurrence of postoperative complications in the patient group analysed.

Conclusion: In CD patients undergoing ileocecal resection, no blood transfusion and low preoperative cholesterol levels were associated with unfavourable postoperative outcome. Intra-abdominal abscess discovered during surgery and laparotomy were correlated with longer stay in hospital.

Disclosure: Nothing to disclose

P0472

PREVALENCE AND PREDICTIVE FACTORS OF FATIGUE IN INFLAMMATORY BOWEL DISEASE PATIENTS IN REMISSION

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Introduction: Even in remission, fatigue is a common symptom faced by patients with inflammatory bowel disease (IBD). The object of our study is to determine factors associated with high levels of fatigue in patients with IBD in remission and investigate its prevalence.

Aims & Methods: IBD patients in remission presented at our gastroenterology unit during last three months were colliged. Patients complete Functional Assessment of Chronic Illness Therapy-Fatigue score (FACITC-F). The Fatigue subscale (FS) was the main item used. Scores range from 0 to 52. Fatigue was determined as FS less than 40 points. A score of less than 20 points indicates severe fatigue. We used medical records to abstract demographic and disease characteristics of the participants.

Results: Seventy four patients (85.1% Crohn's Disease (CD) patients and 14.9 % ulcerative colitis (UC)) were included in this study. There were almost same number of man and female in our study (42% vs 58%), with a median age of 26.7 years. The prevalence of fatigue in the analysed group was 54.7%. Ten percent of patients had severe fatigue. Anaemia (p=0.2) and iron deficiency (p=0.61) are not significantly associated with high levels of fatigue. Lower cholesterol level (p=0.013) and higher C-reactive protein value (p=0.04) were risk factors of increased fatigue. Multiple bowel resections presents strong associations with fatigue (p=0.01). Extra-intestinal manifestations were significantly associated with fatigue (p=0.008). We detected that perianal CD induces high fatigue (p= 0.022). We observed that 65% of patients with perianal CD did not answer sexuality item.

Conclusion: Even in remission, IBD patients suffer from fatigue. Multiple bowel resections, extra-intestinal manifestations, high C-reactive protein and cholesterol level were risk factors of fatigue. Patients with perianal CD had greater fatigue levels, which allows us to think that they are unsatisfied with their sexual lives.

Disclosure: Nothing to disclose

P0473

THE SIMPLIFIED MARIA SCORE IS STRONGLY CORRELATED WITH THE MARIA AND CLERMONT SCORES TO ANALYZE THE LUMINAL ACTIVITY OF CROHN'S DISEASE (CD) IN MRI AND IS EASIER TO CALCULATE

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Introduction: Two scores have shown their interest in evaluating the luminal activity of MC in MRI, the MARIA and Clermont scores, but their calculation can be complicated in clinical practice. Recently, the Spanish authors validated a new simplified MARIA score and retrospectively showed a very good correlation with the initial MARIA score.

Aims & Methods: The purpose of this study was to validate this correlation in an independent cohort and to compare its feasibility with other scores.

Patients and methods: This was a retrospective analysis of all entero-MRIs performed in our department to evaluate the luminal activity of CD. Two independent radiologists each calculated the MARIA, Clermont and simplified MARIA (MARIAS) scores, each blind to the other and blind to clinical activity (wall thickness > 3mm, oedema, comb sign, ulcerations). In case of disagreement between the two radiologists, a third reader analyzed the MRI enterologist. Correlations were calculated between these three tests for the entire cohort. In addition, concordance tests were performed for predetermined thresholds of 7 to 11 for the MARIA score, 8.5 to 12.5 for the Clermont score and 1 to 2 for the MARIAS score. The duration of the analysis was reported for each reading. Pure colic forms of CD were excluded from the study.

Results: 121 MC were included (65 in clinical and biological activity, 33% pure ileo-colonic 67%, mean age: 38.5 years, sex ratio M/F=54.5%). The agreement between the MARIA score between 7 and 11, the Clermont score between 8.5 and 12.5 and the MARIAS score between 1 and 2 was 0.92 (Fleiss kappa test). The correlation between the MARIA score and its simplified score was very strong (r= 0.93; 95%CI: 0.9 - 0.95) as well as between the Clermont score and the MARIAS score (r= 0.92 95%CI: 0.89 - 0.95). Inter-observer agreement was significantly higher in the calculation of the MARIAS score (96%) compared to 80% for the MARIA and Clermont scores (p=0.04). Reading time was significantly faster for the MARIAS score (3.45+/-0.4 min) compared to the MARIA (10.05+/-1.2 min) and Clermont (13.5+/-3.5 min) scores (p<0.01). Positive predictive values for deep remission (clinical remission and calprotectin < 250 µg/g stool) were 95% at thresholds <1, <7 and <8.5 for the MARIAS, MARIA and Clermont scores, respectively.

Conclusion: In this independent cohort, we confirm the very strong correlation between the simplified MARIA score and the two reference scores (MARIA and Clermont) in the analysis of MC luminal activity as well as its rapid calculation and strong inter-observer agreement. This score, which is simple to achieve in clinical practice, could be systematically calculated by radiologists, allowing for quantifiable monitoring.

Disclosure: Nothing to disclose

P0474

GASTROINTESTINAL ULTRASOUND PERFORMED ON ADMISSION PREDICTS THE NEED FOR INPATIENT INFLIXIMAB THERAPY IN HOSPITALISED ULCERATIVE COLITIS PATIENTS

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Introduction: Patients admitted to hospital with a flare of ulcerative colitis (UC) requiring intravenous corticosteroids are assessed at day three for response, and the need for salvage therapy (usually with infliximab) is determined. Early predictors of likelihood of response help plan for care.

Aims & Methods: To determine if gastrointestinal ultrasound (GIUS) performed early in hospital admission can predict steroid-refractory UC requiring salvage therapy.

A pilot study was conducted. Ten sequential patients requiring admission to hospital for intravenous corticosteroids with confirmed or suspected UC were included. GIUS was performed within 24 hours of admission with a faecal calprotectin. A detailed record of patient characteristics, daily assessment, progress, management and routine investigations (including

endoscopic assessment) was maintained. During the inpatient stay, GIUS was repeated on Day 3 and Day 7 (where appropriate). GIUS assessment was completed by two gastroenterologists. Each colonic segment was assessed: four measurements of bowel wall thickness (BWT), hyperaemia using the Limberg score¹, wall stratification (normal, reduced, absent), presence of lymphadenopathy and mesenteric hyperechogenicity, and loss of haustration (yes or no). BWT was derived from the mean of the 8 measurements obtained, four from each gastroenterologist. Of the categorical variables, the most severe assessment or highest grade from the two gastroenterologists was used for analysis. The colonic segment was considered affected, if the BWT was ≥ 4 mm. The data were analysed with GraphPad Prism 8.

Results: Patient demographics: The mean age was 29.5 years (90% male). 50% were known UC and 50% were newly diagnosed. Based on Truelove and Witts' criteria², 80% had severe disease and 20% moderate. The median C-reactive protein on admission was 65 (10-255) mg/L and the median faecal calprotectin was 1653 (1048-5895) $\mu\text{g/g}$. Six of the ten patients required salvage therapy within 3 (3-7) days, all treated with infliximab, of whom four received escalated dosing.

GIUS findings: On admission, the median colonic BWT was lower in the steroid responders 4.6 (4.2-5.6) mm compared with 6.2 (6-7.9) mm in the steroid non-responders who required infliximab ($p=0.009$; Mann-Whitney U test). Furthermore, individuals who had any colonic segment with a BWT >6 mm were more likely to require infliximab, whereas individuals with all colonic BWT <6 mm were more likely to be steroid responsive, 100% vs 25% ($p=0.033$; Fisher's exact test). There was no association between the median Limberg score of the affected bowel segments ($p=0.5$; Mann-Whitney U test) or the number of colonic segments recorded with severe hyperaemia (Limberg 4) ($p=0.27$; Mann-Whitney U test) and the need for salvage therapy. Preserved wall stratification ($n=3$) compared with reduced or absent wall stratification ($n=7$) was not associated with steroid responsiveness ($p=0.5$; Fisher's exact test). Lymphadenopathy, mesenteric hyperechogenicity and loss of haustration were seen in all patients on day 1. Unsurprisingly, the Day 3 median BWT also predicted the need for salvage therapy, with the median BWT 4 (3.5-4.5) mm in those who responded to steroids and 6.3 (5.5-6.9) mm in those who received infliximab ($p=0.009$; Mann-Whitney U test).

Conclusion: GIUS at admission can predict steroid-refractory disease and the need for salvage therapy in individuals who require admission for a flare of UC. Consideration should be given to performing GIUS on admission to hospital, where available, to risk-stratify patients.

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Disclosure: Nothing to disclose

P0475

DIFFUSION-WEIGHTED MAGNETIC RESONANCE ENTEROCOLONOGRAPHY AND CDEIS IN ASSESSING CROHN'S DISEASE ACTIVITY

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Introduction: Crohn's disease (CD) usually affects young adults and can have a progressive and disabling course. Therefore early diagnosis and monitoring of activity are essential. The development of magnetic resonance imaging (MRI) sequences in the last decade has made MRI of the bowel a very attractive diagnostic tool of CD. Magnetic resonance enterocolonography (MR-EC) is a non-invasive imaging modality that complements ileocolonoscopy. The diffusion-weighted imaging (DWI) creates contrast through the motion of water and other small molecules with tissue, which allows qualitative and quantitative functional analysis. The sequence is non-time consuming, and the most significant advantage is that no intravenous contrast is needed. Different pathological features, such as cell density, extracellular matrix, nucleic acids, and membrane permeability, can be assessed by DWI quantified with an apparent diffusion coefficient (ADC).

Aims & Methods: This study aimed to determine the potential of DWI in the evaluation of patients with CD as a new opportunity to extend MR-EC capacity by comparing DWI with endoscopic activity index.

Overall, 229 patients with suspected CD prospectively underwent magnetic resonance enterocolonography (MR-EC) with DWI sequence and ileocolonoscopy. CD endoscopic index of severity (CDEIS) was calculated.

Results: Of the 229 investigated patients, the clinical diagnosis of CD was confirmed in 100 persons. Using a receiver operating characteristic curve, we showed that DWI score ≥ 2 had 96.9% sensitivity and 82.3% specificity for diagnosing CD. A threshold ADC value of $1.30 \times 10^{-3} \text{ mm}^2/\text{s}$ can distinguish between healthy and inflamed bowel segments with a sensitivity of 73.8% and a specificity of 98% using the Copenhagen diagnostic criteria as a reference standard.

According to endoscopy, 20 (20%) patients were with inactive disease (CDEIS < 3), 59 (59%) had mild disease (CDEIS 3-8), and 21 (21%) patients had the moderate-severe disease (CDEIS ≥ 9).

With the increasing activity of CD, a significant increase in the DWI signal intensity score was observed, and the ADC values decreased. There were significant differences in the DWI scores and ADC values comparing patients with inactive, mild, moderate-severe disease ($P < 0.005$).

Conclusion: DWI is a valuable tool that is able to discriminate between mild and moderate and severe CD activity.

Disclosure: Nothing to disclose

P0476

INTESTINAL ULTRASOUND IN ULCERATIVE COLITIS PATIENTS TREATED WITH TOFACITINIB PREDICTS ENDOSCOPIC OUTCOMES, A LONGITUDINAL PROSPECTIVE COHORT STUDY

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Introduction: Intestinal ultrasound (IUS) shows strong correlation with endoscopy when evaluating disease activity in UC¹. However, only few studies used IUS to assess treatment responses in UC². We aimed to evaluate IUS parameters to determine treatment outcomes in UC patients starting tofacitinib treatment using endoscopy as the reference standard.

Aims & Methods: Patients with moderate to severe UC (endoscopic Mayo (EMS) score ≥ 2) and disease extension beyond the rectum starting tofacitinib 10 mg BID treatment were included. At baseline and at 8 weeks, disease activity was evaluated using the Simple Clinical Colitis Activity Index (SCCAI), faecal calprotectin (FCP) levels, endoscopy and IUS. During IUS and endoscopy, the colon was assessed per segment (sigmoid colon (SC) and descending colon (DC)) for EMS³ and for bowel wall thickness (BWT), hypervascularity (Limberg score⁴ wall layer stratification (WLS) and haustriation (preserved or lost). At 8 weeks, clinical remission (SCCAI ≤ 5), biochemical remission (FCP ≤ 250 mg/kg), endoscopic remission (EMS of 0), endoscopic improvement (EMS ≤ 1) and endoscopic response (decrease of EMS ≥ 1 point) was assessed. Statistical analysis was performed using a linear mixed model for repeated measurements. Area under the ROC (AUROC) was used to determine optimal cut-off values. Correlation coefficients were analyzed with a Spearman correlation coefficient.

Results: Sixty percent, 31.6% and 21.1% of patients (n=23) achieved clinical, biochemical and endoscopic remission after 8 weeks treatment, respectively. Analysis per segment showed 37% and 47% of patients achieving endoscopic remission and 50% and 60% showed an endoscopic response in the SC and DC, respectively. Patients with an EMS ≥ 2 at baseline and at 8 weeks had increased BWT in the SC (mean: 5.05 ± 1.63 mm) and DC (mean: 5.16 ± 1.56 mm). BWT decreased with 2.45 mm (95% CI 1.36-3.54 mm, $p < 0.0001$) in the SC and 2.60 mm (95% CI 1.67-3.53 mm, $p < 0.0001$) in the DC when there was endoscopic response in the corresponding segment. Cut-off values of BWT for segmental endoscopic remission and improvement are demonstrated in Table 1.

	Cut-off value BWT for SC in mm	Cut-off value BWT for DC in mm
Endoscopic remission (EMS=0)	≤ 3.35 (AUROC: 0.90, sensitivity: 79% specificity: 87%, $p < 0.0001$)	≤ 2.63 (AUROC: 0.97, sensitivity: 96% specificity: 92%, $p < 0.0001$)
Endoscopic improvement (EMS ≤ 1)	≤ 3.90 (AUROC: 0.90, sensitivity: 82%, specificity: 86%, $p < 0.0001$)	≤ 3.34 (AUROC: 0.92 sensitivity: 88%, specificity: 89%, $p < 0.0001$)
Clinical remission (SCCAI ≤ 5)	≤ 3.90 (AUROC: 0.82, sensitivity: 80% specificity: 75%, $p = 0.001$)	≤ 3.00 (AUROC: 0.78, sensitivity: 68% specificity: 71%, $p = 0.005$)
Biochemical remission (FCP ≤ 250 mg/kg)	≤ 3.90 (AUROC: 0.81, Sensitivity: 71% specificity: 89%, $p = 0.005$)	≤ 2.63 (AUROC: 0.75, sensitivity: 71% specificity: 71%, $p = 0.038$)

[Table 1: cut-off values for BWT in SC and DC indicating segmental endoscopic response and improvement, clinical remission and biochemical remission]

There was a strong correlation for the EMS and BWT ($p = 0.66$, $p < 0.0001$), hypervascularity ($p = 0.70$, $p < 0.0001$), WLS ($p = 0.52$, $p = 0.001$) and haustriations ($p = 0.73$, $p < 0.0001$). Hypervascularity, WLS and haustriations nor-

malized in patients achieving endoscopic remission in the SC ($p < 0.0001$, $p = 0.035$, $p = 0.001$) and DC ($p < 0.0001$, $p = 0.001$, $p < 0.0001$). Cut-off values for BWT in patients achieving clinical and biochemical remission are demonstrated in Table 1.

Conclusion: IUS accurately detected treatment responses during 8 weeks treatment with tofacitinib in UC patients and showed strong correlation with clinical, biochemical and endoscopic outcomes. Hence, this non-invasive and highly accurate imaging technique should be incorporated in standard care in order to closely monitor such patients.

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Disclosure: Nothing to disclose

P0477

MACHINE LEARNING AS A DECISION-SUPPORT TOOL FOR SELECTING PATIENTS WITH CROHN'S DISEASE FOR ABDOMINOPELVIC CT IN THE EMERGENCY DEPARTMENT

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Introduction: Patients with Crohn's disease (CD) presenting to the emergency department (ED) for disease exacerbation frequently undergo abdominopelvic computed tomography (APCT) in order to detect CD related complications [1]. Repeated CT scans lead to increased ionizing radiation exposure. Therefore, there is a need to identify patients with higher probability of finding a CD-related complication evident in APCT in the ED [2,3]. We explored the use of machine learning (ML), an artificial intelligence (AI) derived method [4], for constructing a decision-support tool to select patients at high or low risk for CD related complications on APCT in the ED.

Aims & Methods: We performed a retrospective cohort study at Rabin Medical Center, a tertiary referral center for patients with IBD in Israel. Electronic medical records (EMR) of patients with CD who presented to the ED for gastrointestinal complaints and who underwent APCT were reviewed. Complications on CT scans were defined as bowel obstruction, perforation, intra-abdominal abscess, or complicated fistula (enterovesicular or enterocutaneous). CT scan reports were evaluated independently by three physicians, using a voting system to ensure accurate classification of findings. ML was used to construct a model to predict complications on APCT, based on routine clinical variables available in the ED. We trained and cross-validated different popular ML classifiers and calculated the sensitivity, specificity, and area under the operator receiving characteristic (AUROC) curve in order to choose the best model.

Results: A total of 362 ED admissions of patients with CD were screened with 101 fitting the inclusion criteria. Fifty-one (50.4%) cases had a complication on APCT. Out of 30 clinical variables documented, the model rel-

duced the variables used as features to a final eight variables (Table 1). The Random Forest model was chosen as the best model. The model was able to identify a group of patients at low risk for complications with a negative predictive value (NPV) of 95.2%. The model also identified a group of patients at high risk for complications with a positive predictive value (PPV) of 84.2%. This allowed us to construct a risk stratification system comprised of 3 categories: high-risk patients (94% probability for complications), medium risk, and low-risk (>98% probability of not having any complications) table 2. Based on this risk stratification, patients in the low-risk category may be safely spared an APCT, whereas in patients belonging to the high-risk category APCT is highly recommended. For patients with medium risk, a more individualized decision-making process should be undertaken. Applying the model is expected to reduce the APCT's in the cohort by 20%.

Conclusion: We present a novel AI-based decision-support tool, utilizing eight readily available clinical variables to better select patients presenting with CD related acute GI complaints for APCT in the ED. This approach might reduce the number of APCTs performed for low-risk patients, thus avoiding unnecessary ionizing radiation and contrast material while ensuring high-risk patients undergo APCT in the ER. If validated in prospective studies this may be used for improving efficient treatment and safety of patients with CD.

Cutoff boundary	Risk category	Performance	Suggested action
<0.2	Low risk	Sensitivity 98.04% NPV 95%	Avoid APCT
0.2-0.8	Medium risk	Sensitivity 76.47% Specificity 72%	Consider APCT according to individual case
>0.8	High risk	Specificity 94% PPV 84.2%	Proceed to APCT

[Model results, patient risk stratification and suggested clinical action]

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Disclosure: Nothing to disclose

P0478

BIOMARKERS OF EXTRACELLULAR MATRIX REMODELLING ARE ASSOCIATED WITH INTESTINAL FIBROSIS ASSESSED BY MAGNETIC RESONANCE ENTEROGRAPHY AND ACCUMULATED INTESTINAL DAMAGE (LÉMANN INDEX) - THE IBSEN STUDY

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Introduction: Magnetic Resonance Enterography (MRE) has become an important tool in the diagnosis and follow-up of Crohn's disease (CD). MRE findings are used in the calculation of the Lémann index (LI), a score that quantifies accumulated bowel damage. However, calculating the score is demanding; thus, serum biomarkers reflecting tissue damage and fibrosis are warranted for monitoring purposes. Increased extracellular matrix (ECM) remodeling and collagen tissue deposition is the result of accumulated bowel damage, eventually leading to intestinal fibrosis; particularly, the basement membrane and interstitial matrix are affected. We aimed to investigate ECM serum biomarkers of type III collagen formation (PRO-C3), type IV collagen degradation (C4M), degradation of citrullinated vimentin (VICM) and their association with LI and the degree of bowel wall fibrosis assessed by contrast-enhanced MRE in CD patients.

Aims & Methods: Serum from CD patients was analysed (n=85, part of IBSEN population). Competitive ELISA was applied for the quantification of PRO-C3, C4M and VICM in the serum samples. The LI score was calculated based on the surgical history, MRE findings and the endoscopy findings. The suggested cut-off for substantial bowel damage is LI $\geq$ 2. Increased contrast enhancement of the bowel wall at 5 minutes and the presence of stenosis on MRE was considered severe fibrosis. Student's t-test, Spearman's r correlation and One-way-ANOVA with FDR correction was applied for statistical analysis.

Results: Serum levels of C4M were elevated in patients with confirmed fibrosis by contrast MRE compared to patients without fibrosis (P=0.031, AUC:0.61) (figure 1A). VICM correlated to the LI score in CD patients (r=0.26, P=0.015) and serum VICM levels were elevated in patients with a LI score $\geq$ 2 (P=0.005, AUC: 0.67) (figure 1B). VICM was significantly associated with intestinal damage for LI $\geq$ 20 (LI 0 vs. $\geq$ 20: P=0.005, AUC: 0.72). PRO-C3 was not associated with intestinal damage or intestinal fibrosis.

Conclusion: Our results indicate that the accumulated intestinal damage and the bowel wall fibrosis in CD are associated with elevated serum levels of VICM and C4M respectively. Thus, serological biomarkers of basement membrane degradation and inflammation may be useful tools to monitor intestinal tissue damage and fibrosis development.

Disclosure: JHM, TMJ, MAK, MJN, DJL, are full time employees at Nordic Bioscience. MAK and DJL holds stocks in Nordic Bioscience

P0479

COMPARISONS OF DIFFERENT MRI SCORES TO DEFINE THERAPEUTIC RESPONSE IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Transmural healing assessed using MRI is a promising therapeutic goal in patients with Crohn's disease as it is associated with long-term improved outcomes. However, the best definition of therapeutic response, which should predict favorable long-term outcomes, be highly sensitive to change and be accessible by a significant proportion of patients with the current medications, remains unknown.

Aims & Methods: We compared the five MRI scores or indices available in CD to predict long-term favorable outcomes, to be sensitive to change after treatment and to be reached by the current medications. We also assessed the collinearity of the items including in each score.

From a database including all the consecutive patients who performed an MRI to assess luminal CD between January 2012 and June 2018 in our IBD unit, we selected all the patients with CD (> 18 yearsold) who underwent two MRI with:

- 1) objective signs of inflammation on the 1st MRI,
- 2) the second MRI performed to assess therapeutic efficacy,
- 3) follow-up > 6 months and no surgery between the two MRI.

All the patients underwent MRI assessing the small bowel and the colon using a standardized protocol (no bowel cleansing the day before and no colonic distension). MaRIA, simplified MaRIA, Clermont score, Nancy score and London index were calculated as previously published. Sensitivity to change was assessed by calculating the standardized mean difference (SMD).

Results: Overall, 443 patients undergoing 889 MRI were screened for the study. Among them 274 patients were included (mean age 33.1 ± 15.8 years, median CD duration = 7.0 [2.013.0] years, 36.4 % smokers, 31.4 % prior intestinal resection, L1 = 51.5 %, L2 = 5.5 % and L3 = 43.1 %, 25.9 % perianal lesions, 35.4 % stricturing CD and 31.0 % fistulizing CD). At the time of the second MRI, the patients received one or several medications among: steroids (6.3 %), immunosuppressants (45.2 %), anti-TNF agents (65.7 %) or ustekinumab (2.6 %). The median interval between the 2 IRM was 9.2 months [6.0 - 14.1]. Among all the thresholds of the investigated scores, only the following endpoints were associated with decreased risk of surgery: Δ MaRIA $\geq$ 50% (HR: 0.10 p=0.034 [0.01-0.84]), MaRIA < 7 (HR: 0.14 p=0.071 [0.02-1.19]), Δ Clermont score $\geq$ 25% (HR: 0.31 p=0.037 [0.12-0.93]) or $\geq$ 50% (HR: 0.11 p=0.038 [0.13-0.88]), Clermont score < 8.4 (HR: 0.12 p=0.047 [0.014-0.97]) or < 12.5 (HR: 0.11 p=0.041 [0.01-0.91]), Δ London index $\geq$ 25% (HR: 0.06 p=0.012 [0.01-0.55]), Δ Nancy score $\geq$ 25% (HR: 0.08 p=0.017 [0.01-0.63]), Δ Nancy score $\geq$ 50% HR: 0.11 p=0.043 [0.01-0.94]), Nancy score $\leq$ 2 (HR: 0.11 p=0.044 [0.01-0.94]), Δ Nancy score $\leq$ 3 (HR: 0.07 p=0.013 [0.01-0.57]). Simplified MaRIA did not predict the risk of surgery. Therapeutic response was achieved in 21% of the patients using Δ Clermont score $\geq$ 25%, in 17 % with Δ London index $\geq$ 25%, and in 14 % with Δ Nancy score $\geq$ 50%. All the other endpoints were reached by less than 12% of the patients. Among these scores, the best sensitivity to change was observed in Clermont score (SMD = 0.6), Nancy score (SMD = 0.54) and MaRIA (SMD=0.48). A significant collinearity was observed between the following MRI lesions: ulceration, edema, increased bowel enhancement meaning that these items give nearly the same information.

Conclusion: In this large cohort of patients, we provided helpful information to choose the best definition of therapeutic response using MRI scores both in daily practice and clinical trials.

Disclosure: Nothing to disclose

P0480

THERAPEUTIC DRUG MONITORING DOSING REGIMEN WITH ADALIMUMAB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE SERENE-UC MAINTENANCE STUDY

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Introduction: Adalimumab (ADA) is efficacious and well tolerated in adult patients (pts) with ulcerative colitis (UC).^{1,2} SERENE-UC (NCT02065622) evaluated higher ADA dosing regimens for induction and maintenance in UC. Results of the fixed-dosed maintenance arms have been previously reported.^{3,4} Here, we report the outcomes of adjusting ADA dosing based on proactive monitoring of ADA serum levels and symptoms in the therapeutic drug monitoring (TDM) exploratory maintenance arm.

Aims & Methods: SERENE-UC was a Phase 3 study in adult pts with moderately to severely active UC. Following completion of the induction study at Week (Wk) 8, all pts were re-randomized 2:2:1 to 44 weeks of maintenance therapy with either ADA 40 mg every week (40EW), ADA 40 mg every other week (40EOW), or exploratory TDM regimens. Pts were stratified by induction regimen, clinical response status at Wk8, and clinical remission (CRem) status at Wk8 among Wk8 responders. All pts in the TDM arm received ADA 40 mg at Wk8 and Wk10; ADA dosing could be escalated to 40EW at Wk12, Wk24, or Wk37, followed by a single dose of 160 mg at Wk24 or Wk37 and 40EW from the following week if pts met the dose-adjustment criteria (Rectal Bleeding Subscore $\geq$ 1 and/or ADA serum concentration < 10 µg/mL, as measured at the prior study visit). The endoscopic component of the Mayo score was scored via central reading. The TDM regimen was exploratory, and only descriptive statistics have been provided. Safety was assessed throughout.

Results: Overall, 757/852 pts completed induction and were re-randomized at Wk8; 151 pts were included in the TDM arm. At Wk52, 36.5% (n=27/74) of Wk8 responders in the TDM arm achieved CRem, while 23.2% (35/151) of all pts and 10.4% (8/77) of Wk8 non-responders receiving TDM were in CRem. The proportion of Wk8 responders who completed Wk52 and were escalated to TDM 40EW increased over time (Table); at Wk52, 83.6% (46/55) of pts had received 40EW. Based on the dose received at the

Wk37 decision point, mean (SD) serum drug levels at Wk52 for the TDM 40EW, TDM 40EOW, and TDM 160 mg to 40EW regimens were 19.0 (8.2) $\mu\text{g/mL}$, 13.9 (4.0) $\mu\text{g/mL}$, and 10.3 (7.8) $\mu\text{g/mL}$, respectively. Of the 71 pts who had a dose escalation, 65% (46/71) were driven solely by an ADA serum concentration of $< 10 \mu\text{g/mL}$ (Table). The safety profile of the TDM arm was consistent with the EW and EOW maintenance arms⁴; the rates of treatment-emergent infections and serious infections were 33.8% and 2.0%, respectively.

Conclusion: Data from the SERENE-UC TDM exploratory arm showed that during 44 weeks of maintenance treatment, a majority of patients escalated ADA to 40 EW, and this was driven mainly by ADA serum levels. No new long-term safety concerns were observed in the TDM maintenance arm, and the observed safety profile was comparable with the known safety profile of the EOW maintenance regimen.⁴

	Wk12 (sample taken at Wk10)	Wk24 (sample taken at Wk22)	Wk37 (sample taken at Wk35)
Dose-adjustment outcome in Wk8 responders who completed Wk52 of the TDM arm			
ADA 40 mg EW, n/N (%)	22/55 (40.0)	31/55 (56.4)	33/55 (60.0)
ADA 40 mg EOW, n/N (%)	33/55 (60.0)	12/55 (21.8)	9/55 (16.4)
ADA 160 mg to ADA 40 mg EW, n/N (%)	—	12/55 (21.8)	13/55 (23.6)
Factors driving dose escalation in pts who received a dose escalation in the TDM arm ^a			
Only Rectal Bleeding Subscore ≥ 1 , n/N (%)	4/22 (18)	3/33 (9)	1/16 (6)
Only ADA serum concentration $< 10 \mu\text{g/mL}$, n/N (%)	16/22 (73)	21/33 (64)	9/16 (56)
Rectal Bleeding Subscore ≥ 1 and ADA serum concentration $< 10 \mu\text{g/mL}$, n/N (%)	2/22 (9)	7/33 (21)	3/16 (19)

^a2 and 3 pts were dose escalated
at Wk24 and Wk37 without
meeting criteria, respectively.

[Table. Dose-adjustment outcome and factors driving dose escalation]

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P0481

EARLY AND DURABLE SYMPTOM CONTROL IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS TREATED WITH ETASIMOD (APD334) IN THE RANDOMISED, DOUBLE BLIND, PLACEBO CONTROLLED, PHASE 2 OASIS TRIAL AND OPEN LABEL EXTENSION

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Introduction: Etrasimod is a once daily, oral, selective sphingosine 1-phosphate receptor modulator with efficacy in the 12-week OASIS trial (NCT02447302) in adult patients with moderately to severely active ulcerative colitis (UC).^{1,2} Patients who completed the double blind (DB) study were eligible to enrol in an open label extension (OLE; NCT02536404) and received etrasimod 2 mg once daily for ≥46 or 52 weeks total (71% or 21%, respectively).³ In the OLE, etrasimod 2 mg demonstrated sustained benefit, with clinical response, endoscopic improvement, and clinical remission at end of treatment (EOT) in 93%, 77%, and 75% of patients with each respective status at Week 12 who received etrasimod 2 mg in the DB study and OLE and who completed the OLE.³

Aims & Methods: In this study we evaluated the association between improvement in the patient-reported outcomes of rectal bleeding (RB) and stool frequency (SF)⁴ and clinical and endoscopic response at EOT in patients receiving etrasimod 2 mg. We calculated least squares mean (LSM) reductions in RB and SF over time in patients receiving etrasimod 2 mg (n=49) or placebo (PBO; n=52) in the DB study and mean reductions in RB and SF over time in patients receiving etrasimod 2 mg throughout the DB study and OLE (treat-through group, n=31). The analyses included patients with non-missing assessments and used Mayo Clinic subscores (range 0-3). Endoscopic improvement was an endoscopic subscore ≤1; clinical remission was endoscopic improvement, RB score ≤1, and SF score ≤1 with ≥1 point decrease from DB baseline; clinical response was clinical remission or a decrease in modified Mayo Clinic score (endoscopy, RB, SF) of ≥2 and ≥30%, with RB score ≤1 or ≥1 RB decrease.

Results: During the DB study, patients receiving etrasimod 2 mg had a significantly greater LSM (standard error [SE]) reduction in RB versus PBO at Week 2 (etrasimod 2 mg, 0.55 [0.10], P=0.016; PBO, 0.26 [0.10]) that continued through Week 12 (etrasimod 2 mg, 0.97 [0.12], P=0.025; PBO, 0.63 [0.12]). Compared with PBO, patients receiving etrasimod 2 mg had a numerically greater LSM (SE) reduction in SF as early as Week 2 (etrasimod 2 mg, 0.33 [0.11], P=0.226; PBO, 0.22 [0.11]) that continued to Week 12 (etrasimod 2 mg, 0.74 [0.14], P=0.237; PBO, 0.61 [0.13]). At EOT, patients in the etrasimod 2 mg treat-through group had no change in mean (SE) reductions of RB (0.0 [0.12], P=0.769) or SF (0.1 [0.18], P=0.558) compared with Week 12. In the etrasimod 2 mg treat-through group, reductions in RB and SF were greater in patients with clinical response or clinical remission at EOT versus without (Table). Reduction in SF was greater in patients in the treat-through group who had endoscopic improvement at EOT versus those who did not.

Conclusion: Patients with UC who received etrasimod 2 mg in the OASIS clinical trial and its OLE had early and durable clinical improvements seen as soon as Week 2. Patients had long-term clinical and endoscopic improvement and experienced associated long-term symptomatic improvement.

	Clinical Response:		Endoscopic Improvement:		Clinical Remission:	
	No	Yes	No	Yes	No	Yes
RB						
At Week 12	-0.77 (0.26)	-1.39 (0.16) P = 0.042	-0.89 (0.20)	-1.50 (0.19) P = 0.051	-0.85 (0.20)	-1.64 (0.15) P = 0.011
At EOT	-0.7 (0.26)	-1.50 (0.15) P = 0.007	-1.00 (0.20)	-1.50 (0.19) P = 0.097	-0.94 (0.20)	-1.64 (0.15) P = 0.019
SF						
At Week 12	-0.54 (0.22)	-1.39 (0.24) P = 0.0187	-0.63 (0.17)	-1.67 (0.31) P = 0.004	-0.60 (0.17)	-1.82 (0.30) P ≤ 0.001
At EOT	-0.1 (0.31)	-1.89 (0.20) P ≤ 0.001	-0.69 (0.30)	-2.00 (0.25) P = 0.003	-0.65 (0.28)	-2.18 (0.18) P ≤ 0.001

Data are mean (SE) change from baseline with nominal P value determined by t-test of status (No versus Yes).

[Change in rectal bleeding and stool frequency in patients receiving etrasimod 2 mg in the DB study and OLE by efficacy status at EOT (n=31)]

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P0482

EXPOSURE-RESPONSE RELATIONSHIP OF SUBCUTANEOUS INFLIXIMAB (CT-P13 SC) IN PATIENTS WITH ACTIVE CROHN'S DISEASE AND ULCERATIVE COLITIS: ANALYSIS FROM A MULTICENTER, RANDOMIZED CONTROLLED PIVOTAL TRIAL

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Introduction: Subcutaneous formulation of infliximab (CT-P13 SC) was developed to provide flexible therapeutic use of infliximab in patients with chronic autoimmune diseases. CT-P13 SC demonstrated non-inferiority in maintenance pharmacokinetics (C_{trough}), and suggested similar efficacy and safety compared to the intravenous (IV) CT-P13 in patients with active Crohn's disease (CD) and ulcerative colitis (UC).¹

Aims & Methods: Data from infliximab naïve patients who received CT-P13 SC maintenance treatment (SC arm) in the randomized controlled pivotal trial for active CD (Crohn's Disease Activity Index [CDAI] score of 220 to 450) and UC (total Mayo score of 6 to 12 with endoscopic subscore of ≥ 2) were analyzed for exposure-response relationships. Loading doses of CT-P13 IV 5 mg/kg were administered at Weeks 0 and 2. From Week 6, patients

who were randomized to the SC arm received maintenance treatment of CT-P13 SC 120 mg (< 80 kg at Week 6) or 240 mg (≥ 80 kg at Week 6) every 2 weeks up to Week 54. Associations between pre-dose serum infliximab concentrations and clinical efficacy/ fecal calprotectin (FC) response were investigated, including possible differences between remitter and non-remitter subgroups.

Results: In total, 66 patients (28 CD, 38 UC) were randomized to the SC arm. 55 (83.3%) patients completed the CT-P13 SC maintenance treatment up to Week 54 and 42 (63.6%) patients achieved clinical remission at Week 54. Maintenance treatment of CT-P13 SC resulted in a stable exposure to infliximab with trough drug levels above the generally accepted lower therapeutic margin of $5 \mu\text{g/mL}$ ^{2,3} in 90.9% of the patients (50/55) throughout all observed study visits after initial SC dosing and up to Week 54. Overall mean pre-dose serum drug levels and proportions of patients achieving $\text{FC} \leq 250 \mu\text{g/g}$ were numerically higher in the Week 54 remitters compared to the non-remitters throughout the study. Upon subgrouping patients according to quartiles of drug levels, the proportions of patients achieving efficacy outcomes/ $\text{FC} \leq 250 \mu\text{g/g}$ were the highest in the 4th quartile (TABLE).

There were 31 patients with positive anti-drug antibody (ADA) at Week 54, but only 2 (6.5%) of these patients had concurrent drug level lower than the therapeutic drug level of $5 \mu\text{g/mL}$ ^{2,3}, both with the presence of neutralizing antibodies. All 23 patients with negative ADA had serum drug levels over $5 \mu\text{g/mL}$, and clinical outcomes in patients with or without ADA at Week 54 were not different.

Study Visit	A. Pre-dose IFX levels and fecal calprotectin outcomes at each visit by efficacy at Week 54 ¹	Pre-dose IFX levels ($\mu\text{g/mL}$, mean [SD])	Fecal calprotectin $\leq 250 \mu\text{g/g}$ (n/N [%])	
	Remitters at Week 54 (n=42) ²	Non-remitters at Week 54 (n=12) ⁴	Remitters at Week 54 (n=42) ²	Non-remitters at Week 54 (n=12) ⁴
Week 0	0.0 (0.00)	0.0 (0.00)	6/37 (16.2)	3/12 (25.0)
Week 6	17.0 (9.49)	13.2 (8.43)	19/37 (51.4)	3/10 (30.0)
Week 14	22.9 (9.05)	17.8 (7.24)	26/42 (61.9)	4/11 (36.4)
Week 22	23.5 (9.50)	17.5 (8.44)	23/34 (67.6)	3/9 (33.3)
Week 30	22.9 (9.54) ⁵	16.6 (6.91) ⁵	21/34 (61.8)	6/10 (60.0)
Week 38	23.4 (10.70)	17.5 (8.05)	27/40 (67.5)	6/11 (54.5)
Week 46	23.9 (12.45)	17.5 (8.52)	28/41 (68.3)	6/12 (50.0)
Week 54	25.1 (13.49) ⁵	14.8 (8.24) ⁵	28/37 (75.7)	6/12 (50.0)
B. Clinical outcomes by pre-dose IFX levels quartiles at Week 54, n (%) ²				
	1 st quartile $< 16.4 \mu\text{g/mL}$ (n=13)	2 nd quartile 16.4 to $< 21.5 \mu\text{g/mL}$ (n=13)	3 rd quartile 21.5 to $< 26.7 \mu\text{g/mL}$ (n=13)	4 th quartile $\geq 26.7 \mu\text{g/mL}$ (n=14)
Clinical response ⁶ at both Weeks 30 and 54	9 (69.2)	10 (76.9)	12 (92.3)	13 (92.9)
Clinical remission ⁷ at both Weeks 30 and 54	6 (46.2)	7 (53.8)	10 (76.9)	11 (78.6)
Fecal calprotectin $\leq 250 \mu\text{g/g}$ at Week 54	8/13 (61.5)	9/13 (69.2)	7/11 (63.6)	10/11 (90.9)

1. Among 55 patients who had completed the CT-P13 SC maintenance treatment up to Week 54, 1 patient with missing efficacy assessment result at Week 54 was excluded from the analysis.
2. Among 55 patients who had completed the CT-P13 SC maintenance treatment up to Week 54, 2 patients with missing PK assessment result at Week 54 were excluded from the analysis.
3. CD patients with absolute CDAI score of < 150 points at Week 54 and UC patients with partial Mayo score of ≤ 1 at Week 54 were included in this group.
4. CD patients with absolute CDAI score of ≥ 150 points at Week 54 and UC patients with partial Mayo score of > 1 at Week 54 were included in this group. Ten patients failed to achieve clinical remission at Week 54 in spite of their pre-dose IFX levels $\geq 5 \mu\text{g/mL}$. Of these, 7 patients were non-responders at the start, following the 2 IV loading doses. The rest of the 3 patients had achieved clinical response during the SC maintenance treatment.
5. $p < 0.05$. p -values are based on a comparison of the mean pre-dose concentrations of IFX (t-test) between Week 54 remitters and Week 54 non-remitters.
6. CDAI-100 defined as ≥ 100 points decrease of CDAI score from baseline for CD, ≥ 2 points decrease of partial Mayo score from baseline with ≥ 1 point decrease of rectal bleeding subscore or an absolute rectal bleeding subscore of 0 or 1 for UC.
7. CDAI score of < 150 points for CD, partial Mayo score of ≤ 1 point for UC.

[Infliximab (IFX) exposure and clinical outcomes in patients treated with CT-P13 SC 120/240 mg]

Conclusion: Positive association was demonstrated between the CT-P13 SC exposure and the efficacy/ FC outcomes in patients with active CD and UC. These data support the PK-PD basis for using CT-P13 SC as a novel, convenient and efficacious therapy formulation for CD and UC patients.

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EFFECT OF MIRIKIZUMAB ON INFLAMMATORY BIOMARKERS IN A PHASE 2 STUDY OF PATIENTS WITH CROHN'S DISEASE

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Introduction: Mirikizumab (miri; IL-23p19 antibody) is a humanized, IgG4 monoclonal antibody specifically targeting the p19 subunit of the IL23 cytokine. Prior studies have shown miri to have efficacy in psoriasis, ulcerative colitis, and Crohn's disease (CD). High-sensitivity C-reactive protein (hsCRP) is a known marker of acute inflammation which correlates with disease activity in the majority patients, while fecal calprotectin (FCP) correlates with mucosal inflammation and can be used as a reliable biomarker of mucosal healing¹.

Aims & Methods: At baseline, subjects (N =191) were randomized with a 2:1:1:2 allocation across 4 treatment arms (PBO, 200, 600, 1000 mg miri, administered intravenously (IV) at Weeks 0, 4, 8). Fecal samples and serum were collected for the assessment of FCP and hsCRP, respectively, at baseline (BL) and Week 12. Comparisons to placebo for continuous data were done using the normal approximation for the Wilcoxon two-sample test. For categorical data, a logistic regression analysis was used with treatment, geographic region, and prior biologic CD therapy (prior biologic experience versus prior biologic naive) as factors.

	Placebo (N=64)	Miri 200mg (N=31)	Miri 600mg (N=32)	Miri 1000mg (N=64)
Week 0				
hsCRP (median, Q1, Q3)	6.8 (1.8, 19.0)	7.4 (2.3, 31.4)	6.8 (2.7, 20.7)	4.5 (2.7, 15.5)
FCP (median, Q1, Q3)	799.5 (256.5, 1945.5)	877.0 (225.0, 4359.0)	822.5 (355.0, 2302.5)	773.0 (293.0, 1634.0)
Week 12				
hsCRP % change from BL (median, Q1, Q3)	43.8 (-8.3, 145.5)	-29.9 (-64.8, 25.9)***	-39.8 (-70.6, 0.2)***	-48.6 (-76.1, 35.1)***
FCP % change from BL (median, Q1, Q3)	0.0 (-60.9, 54.1)	-60.7 (-84.8, 68.0)	-62.1 (-84.4, -13.2)**	-76.2 (-90.7, -54.9)***
Patients with normalized hsCRP levels ^a , n (%)	N=44 4 (9.1)	N=23 1 (4.3)	N=23 6 (26.1)*	N=42 14 (33.3)**
Patients with normalized FCP levels ^b , n (%)	N=46 6 (13.0)	N=21 6 (28.6)	N=27 9 (33.3)*	N=49 20 (40.8)**
250 mg/kg	1 (2.2)	3 (14.3)	5 (18.5)**	10 (20.4)**
100 mg/kg	1 (2.2)	2 (9.5)	3 (11.1)	3 (6.1)
50 mg/kg				

^a normal hsCRP level =3 mg/L, N=number of patients with >3 mg/L at baseline; ^b selected cutoffs for normal FCP level = 250, 100, and 50 mg/kg, N=number of patients with >250 mg/kg at baseline; CI=confidence interval; *p<0.1, ** p < 0.05, *** p < 0.001

[Inflammatory Biomarkers After 12 Weeks of Mirikizumab Treatment]

Results: At Week 12, the percent change from BL in hsCRP was significantly greater in all miri groups compared to PBO ([median Q1, Q3] PBO: 43.8 [-8.3, 145.5]; 200mg miri: -29.9 [-64.8, 25.9] p< 0.001; 600mg miri: -39.8 [-70.6, 0.2] p< 0.001; 1000mg miri: -48.6 [-76.1, 35.1] p< 0.001). The percent change from BL in FCP was significantly greater in the 600 and 1000mg miri groups compared to PBO (PBO: 0.0 [-60.9, 54.1]; 200mg miri:

-60.7 [-84.8, 68.0]; 600mg miri: -62.1 [-84.4, -13.2] $p < 0.05$; 1000mg miri: -76.2 [-90.7, -54.9] $p < 0.001$). The percentage of patients with normalized CRP (≤ 3 mg/L) or FCP (≤ 250 , 100, and 50 mg/kg) levels was significantly higher after miri treatment compared to PBO, with the highest proportion of patients in the 1000mg miri group (CRP: PBO 9.1%, 200mg 4.3%, 600mg 26.1% $p < 0.01$, 1000mg 33.3% $p < 0.05$; FCP, 250mg/kg cutoff: PBO 13.0%, 200mg 28.6%, 600mg 33.3% $p < 0.01$, 1000mg 40.8% $p < 0.05$).

Conclusion: The significant and dose dependent decrease of levels of hsCRP and FCP with miri treatment compared to PBO is consistent with results of clinical and endoscopic parameters and demonstrates the anti-inflammatory activity of miri. Notably, substantial proportions of patients had levels in a range observed in healthy subjects.

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AN EXPERT CONSENSUS TO STANDARDIZE THE ASSESSMENT OF HISTOLOGIC DISEASE ACTIVITY IN CROHN'S DISEASE CLINICAL TRIALS

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Introduction: Histologic assessment of intestinal biopsies from patients with Crohn's disease (CD) is required to confirm diagnosis, exclude dysplasia, and evaluate response to treatment. Currently, histology is not recommended as a treatment target in CD clinical trials due to measurement uncertainty and clinical interpretation.

Aims & Methods: We conducted a modified RAND/University of California Los Angeles Appropriateness Methodology (RAM) process to standardize the assessment of histologic disease activity in CD clinical trials. An expert panel of 11 histopathologists and 5 gastroenterologists rated 80 items derived from a systematic literature review and expert opinion on a 1-9 scale. Each item was classified as inappropriate, uncertain or appropriate based on the median panel rating and degree of disagreement (median < 3.5 without disagreement = inappropriate; median 3.5-6.5 or any median with disagreement = uncertain; median > 6.5 without disagreement = appropriate). Disagreement was considered present when 5 or more panelists chose a rating in each extreme 3-point region (1-3 and 7-9).

Results: The panel determined that histologic remission (median = 8 [IQR 6.5-9]) and response (7 [6-8.5]) are appropriate outcomes for clinical trials. Furthermore, there was a preference for separate scoring of the colon and ileum (8 [6-8.5]). A global colonic score, whereby scores from more than one segment of

the colon are combined, was considered an appropriate measure of histologic disease activity in CD. However, the panel was uncertain whether this should be calculated by summing the total score of each segment explored or by dividing the sum of the individual segments by the number of segments explored (6 [5-7]). It was concluded that the endoscopic appearance of the mucosa should guide biopsy site selection, with a minimum of two biopsies taken for each colonic segment (7 [5-8]) and ileum (7 [5-8]). The panel deemed it appropriate to measure degree of architectural changes (7 [5.5-8.5]), lamina propria chronic inflammation (7.5 [6-9]), basal plasmacytosis (7 [6-8]), lamina propria and epithelial neutrophils (9 [8-9]), epithelial damage (8 [7-9]), granulomas (7.5 [5.5-9]) and presence or absence of erosions and ulcers (9 [8-9]). Moreover, absence of neutrophilic inflammation in the mucosa was considered an appropriate histologic target for clinical trials in CD (7 [5.5-8]). The Global Histologic Disease Activity Score (GHAS) (7 [5.5-7]), Geboes Score (7 [5.5-8]), and Robarts Histopathology Index (7 [5.5-8]) were considered appropriate instruments for assessing histologic disease activity in CD. The panel concluded that histologic evaluation in pediatric CD should include biopsies from the upper GI tract.

Conclusion: We evaluated the appropriateness of histologic items related to biopsy collection, diagnosis and treatment targets in CD. These items will be evaluated for intra- and inter-observer reliability and responsiveness, and ultimately used to develop a novel histologic index for use in CD clinical trials.

Disclosure: Nothing to disclose

P0485

DUAL TARGETED THERAPY: A FUTURE STRATEGY FOR THE MANAGEMENT OF REFRACTORY INFLAMMATORY BOWEL DISEASE

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Introduction: Dual Targeted Therapy (DTT) has been proposed as a novel therapeutic strategy for the management of complicated patients with Inflammatory Bowel Diseases (IBD). Our aim was to investigate the safety and effectiveness of this approach in a real-life setting.

Aims & Methods: We retrospectively extracted data from IBD patients receiving DTT in 6 Italian IBD referral centres. Baseline characteristics, clinical activity of intestinal and extraintestinal disease, C-reactive pro-

teins (CRP) levels and endoscopic assessments were recorded. All adverse events were reported. Clinical benefit, defined as "improvement of intestinal and, if appropriate, extraintestinal symptoms after the introduction of DTT", biochemical and endoscopic remission and safety of DTT were the outcomes investigated.

Results: Thirteen patients were identified; indications for DTT were: uncontrolled IBD with no extra-intestinal manifestations (EIM) for 2 patients and concomitant IBD and EIM for 11 patients. In our cohort, patient received: adalimumab (ADA, anti-Tumor Necrosis Factor (TNF) α), certolizumab (anti-TNF), vedolizumab (anti- $\alpha 4/\beta 7$ integrin), ustekinumab (anti-Interleukin (IL) 12/23), secukinumab (anti-IL17) and Apremilast (phosphodiesterase 4 inhibitor). The most commonly used drug was vedolizumab (11 patients, 84.6%); anti-TNF agents were used in 7 (53.8%) patients, followed by ustekinumab in 5 (38.5%); the most common combinations were: vedolizumab + ustekinumab (3 patients, 23.1%) and adalimumab + vedolizumab (3 patients, 23.1%). At baseline, 11/13 (84.6%) and 8/11 (72.7%) patients had active intestinal and extraintestinal symptoms, respectively; 9 (69.2%) patients had elevated CRP and 7 (41.4%) were taking oral steroids. Clinical benefit was observed in 9/13 (69.2%) patients after induction and in 7/8 (87.5%) at 6 months. Clinical response and remission of intestinal symptoms were reported by 5/13 (38.5%) and 4/13 (30.8%) patients at the end of the induction and by 3/8 (37.5%) and 4/8 (50%) at 6 months; clinical response and remission of extraintestinal symptoms were reported by 8/11 (72.7%) and 3/11 (27.3%) patients at the end of the induction and by 3/8 (37.5%) and 5/8 (62.5%) at 6 months. CRP normalization was observed in 9/13 (69.2%) patients at the end of induction and 5/8 (62.5%) at 6 months. Five (71.4%) of the 7 patients taking oral steroids at baseline were able to withdraw them by the end of DTT induction. No patient had to resume corticosteroid treatment while on DTT. Endoscopic assessment was available in 6 patients: one (16.7%) showed endoscopic improvement and 3 (50%) achieved endoscopic remission. Four patients discontinued DTT: 2 because of treatment failure, 1 was lost to follow-up and 1 discontinued due to sustained clinical benefit. Three patients experienced an adverse event; no serious adverse event was reported.

Conclusion: DTT can be considered a reasonably safe and effective treatment in refractory patients.

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IMPROVEMENT OF QUALITY OF LIFE AND CONTINENCE IN PATIENTS WITH DISTAL ULCERATIVE COLITIS TREATED BY MESALAZINE. QUARTZ STUDY

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Introduction: There is no robust data which analyzed quality of life, functional disability and continence of patients with distal UC. QUARTZ is the first prospective study in this situation.

Aims & Methods: Observational, prospective and multicentric study involving public and private French gastroenterologist to recruit patients with mild to moderate (mayo score ≥ 3 and ≤ 10) active proctitis or proctosigmoiditis ($< 20\text{cm}$) and under mesalazine for induction treatment. The patients followed for 12 months (± 2 months). The primary objective was the quality of life evaluated by Short Inflammatory Bowel Disease (SIBDQ) at 8 weeks (± 4 months). The functional disability and incontinence have been evaluated by IBD-Disability Index and Cleveland questionnaires.

Results: From December 2015 to November 2016, 117 patients were recruited. Data of 93 patients have been analyzed and results are reported on table 1. Among the 93 patients, 75 (81%) reached a clinical remission at week 8 with a SIBDQ score improvement of $6,7 \pm 7,1$ point ($p < 0,001$). Treatment adherence during the induction period was non-compliance for 76 patients (81%): 17 (18%) patients stopped treatment before W8 (all those patients received rectal formulation). After induction treatment, 72 (77%) patients received maintenance treatment. 11 (12%) patients reported adverse event not linked to the treatment.

	Mild n=48	Moderate n=45	Total n=93
Gender, M/F	26/22	24/21	50/43
Age, average $\pm$ SD (years)	43,7 $\pm$ 13,6	41,5 $\pm$ 15,6	42,7 $\pm$ 14,5
UC diagnosed < 1 year, n (%)	21(44%)	28(62%)	49(53%)
Oral mesalazine			16(17%)
Topical mesalazine			44(47%)
Oral & local			33(36%)
Combination with steroid	7(15%)	5(11%)	12(13%)
SIBDQ baseline, average $\pm$ SD	40,4 $\pm$ 7,1	35,9 $\pm$ 9,1	38,2 $\pm$ 8,4
SIBDQ week 8	44,8 $\pm$ 6,1*	43,3 $\pm$ 7,6*	44,1 $\pm$ 6,8*
IBD-DI baseline, average $\pm$ SD	21,5 $\pm$ 19,2	32,7 $\pm$ 20,3	26,9 $\pm$ 20,4
IBD-DI week 8, average $\pm$ SD	14,0 $\pm$ 15,3	17,6 $\pm$ 16,0	15,8 $\pm$ 15,7
Cleveland ≥ 4 baseline, n (%)	9(19%)	11(24%)	20(22%)
Cleveland ≥ 4 week 8, n (%)	3(6,3%)	6(13,3%)	9(9,7%)

*p<0.001 vs baseline results

[Table 1: Principals results at baseline and week 8 regarding diseases severity]

Conclusion: For patients with distal ulcerative colitis treated by mesalazine, quality of life, functional disability and continence have been improved at 8 weeks of treatment despite a poor adherence.

Disclosure: I'm medical advisor gastroenterology Ferring France

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SPOSIB SB2 - A SICILIAN PROSPECTIVE OBSERVATIONAL STUDY OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH INFLIXIMAB BIOSIMILAR SB2: FINAL RESULTS

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Introduction: Few data on Infliximab (IFX) biosimilar SB2 in inflammatory bowel disease (IBD) are available.

Aims & Methods: SPOSIB SB2 is a multicenter, observational, prospective study performed among the cohort of the Sicilian Network for Inflammatory Bowel Disease (SN-IBD). All consecutive patients with Crohn's Disease (CD) or Ulcerative Colitis (UC) starting IFX biosimilar SB2 from the introduction of the drug in Sicily (March 2018) to September 2019 (18 months) were enrolled. Patients were divided into five groups (group A: naive to IFX, naive to anti-TNFs; group B: naive to IFX, previously exposed to other anti-TNFs; group C: switch from IFX originator to SB2; group D: switch from CT-P13 to SB2; group E: multiple switches: from IFX originator to CT-P13 to SB2). The primary end-point was the assessment of safety, in terms of rate of serious adverse events (SAEs). Secondary end-point was the evaluation of effectiveness, in terms of steroid-free clinical remission and clinical response at 8 weeks and at the end of follow-up, and as treatment persistency.

Results: 276 patients (median age 39 years; CD 49.3%, UC 50.7%) were included [group A: 127 (46.0%); group B: 65 (23.6%); group C: 17 (6.2%); group D: 43 (15.6%); group E: 24 (8.7%)]. The cumulative number of infusions of SB2 was 1798, the median follow-up was 8 months (IQR: 4-12 months), and the total follow-up time was 182.7 patient-years (PY). Sixty-seven SAEs occurred in 57 patients (20.7%), with an incidence rate of 36.7 per 100 PY, and 26 of them caused the withdrawal of the drug. The incidence rate ratio (IRR) of SAEs was higher among patients in group B compared with group A (57.7 vs. 30.2 per 100 PY; IRR=1.91; p=0.026) and group C (57.7 vs. 18.9 per 100 PY; IRR=2.93; p=0.045). The effectiveness of IFX biosimilar SB2 after 8 weeks of treatment was evaluated in patients naive to IFX (group A + B; n=192): 110 patients (57.3%) had steroid-free remission, 26 patients (13.5%) achieved a partial response, while 56 patients had no response (29.2%). At the end of follow-up, 72 patients (26.1%) interrupted the treatment, without significant differences in treatment persistency estimations between the five groups (log-rank p=0.15).

Conclusion: This is the first prospective study on the use of IFX biosimilar SB2 in IBD. Safety and efficacy of SB2 seem to be overall similar to those reported for IFX originator and IFX biosimilar CT-P13. Multiple switches were safe. A higher incidence of SAEs was observed among patients naive to IFX and previously exposed to other anti-TNFs.

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ASSOCIATION BETWEEN DURATION OF LATEST FLARE BEFORE INDUCTION TREATMENT WITH TOFACITINIB AND EFFICACY OUTCOMES IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). The duration of active disease prior to starting treatment may impact treatment effects. We evaluated the association between duration of the latest flare before starting tofacitinib therapy and efficacy outcomes in the tofacitinib UC clinical programme.

Aims & Methods: Patients (pts) received tofacitinib 10 mg twice daily (BID) or placebo in OCTAVE Induction 1&2 (NCT01465763; NCT01458951) and responders received tofacitinib 5 or 10 mg BID or placebo during OCTAVE Sustain (final efficacy assessment at Week 52; NCT01458574). Pts were stratified by UC flare duration (ie duration of active disease; < 3 and ≥ 3 months) prior to enrolment in OCTAVE Induction 1&2. Differences between the change from baseline Mayo stool frequency subscore (SF), Mayo rectal bleeding subscore (RB) and partial Mayo score (PMS) at Week 2 of OCTAVE Induction 1&2 between flare duration groups were assessed using ANOVA. Associations between flare duration and efficacy endpoints were assessed using the Cochran-Mantel-Haenszel chi-squared test.

Results: Among the 905 pts who received tofacitinib 10 mg BID in OCTAVE Induction 1&2, 443 and 462 pts had flare durations of < 3 months and ≥ 3 months, respectively. A higher proportion of pts with ≥ 3 months of flare duration had pancolitis (53.7%) vs pts with < 3 months of flare duration (48.8%); this was also true for prior tumour necrosis factor inhibitor failure (60% vs 42%). Mean baseline total Mayo score in both groups was 9.0. In OCTAVE Induction 1&2, a numerically higher proportion of pts with < 3 months of flare duration met efficacy endpoints vs pts with ≥ 3 months, with a significant association (Table). Changes from baseline SF, RB and PMS at Week 2 were significantly greater in pts with < 3 months vs ≥ 3 months of flare duration (Table). Among pts who received tofacitinib 5 mg BID in OCTAVE Sustain, a numerically higher proportion of pts with < 3 months of flare duration met efficacy endpoints at Week 52 vs pts with ≥ 3 months; similar proportions of tofacitinib 10 mg BID-treated pts across flare duration groups met efficacy endpoints (Table).

Conclusion: These post hoc analyses showed that latest flare duration was significantly associated with the efficacy of tofacitinib 10 mg BID induction therapy at Week 8, with shorter duration (< 3 months) associated

with greater efficacy, potentially implying that a timely intervention during a new flare may, as expected, lead to a better outcome for induction. During maintenance, flare duration had less impact on efficacy, with similar responses at Week 52 between tofacitinib 10 mg BID groups.

	Flare duration <3 months	Flare duration ≥3 months	p value for change from baseline ^a	p value for association between flare duration and efficacy outcome ^b
Week 2 of OCTAVE Induction 1&2^c				
Change from baseline in Mayo SF subscore, mean (SD)	-0.7 (0.9)	-0.6 (0.8)	0.0117	N/A
Change from baseline in Mayo RB subscore, mean (SD)	-0.8 (0.8)	-0.7 (0.8)	0.0372	N/A
Change from baseline in PMS, mean (SD)	-2.3 (2.0)	-1.9 (1.8)	0.0167	N/A
Week 8 of OCTAVE Induction 1&2^c				
Clinical response, ^d n/N (%)	291/411 (70.8)	230/431 (53.4)	N/A	<0.0001
Mucosal healing, ^e n/N (%)	172/412 (41.7)	99/433 (22.9)	N/A	<0.0001
Remission, ^f n/N (%)	110/412 (26.7)	43/432 (11.3)	N/A	<0.0001
Week 52 of OCTAVE Sustain^c				
Tofacitinib 5 mg BID				
Clinical response, ^d n/N (%)	60/90 (66.7)	28/57 (49.1)	N/A	0.0441
Mucosal healing, ^e n/N (%)	43/90 (47.8)	18/57 (31.6)	N/A	0.0680
Remission, ^f n/N (%)	39/90 (43.3)	16/57 (28.1)	N/A	0.0893
Week 52 of OCTAVE Sustain^c				
Tofacitinib 10 mg BID				
Clinical response, ^d n/N (%)	55/76 (72.4)	49/64 (76.6)	N/A	0.3258
Mucosal healing, ^e n/N (%)	43/76 (56.6)	35/64 (54.7)	N/A	0.6709
Remission, ^f n/N (%)	40/76 (52.6)	29/64 (45.3)	N/A	0.6315

[Table. Efficacy endpoints in the tofacitinib UC clinical programme, by most recent flare duration (FAS, observed)]

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otics, Novo Nordisk, Otsuka, Photopill, Prometheus Laboratories/Nestlé, Progenity, Protagonist, Robarts Clinical Trials, Salix, Sandoz, Seres Therapeutics/Nestlé, SetPoint, Teva, TiGenix, TopiVert and Versant; and lecture fees from Norgine. A Armuzzi has received consultancy fees from Allergan; consultancy and lecture fees from AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Eli Lilly, Ferring, Hospira, Janssen, Mundipharma, Mylan, Roche, Samsung Bioepis, Sandoz and Sofar; research support and consultancy and lecture fees from MSD, Pfizer Inc and Takeda; and lecture fees from AstraZeneca, Chiesi, Mitsubishi Tanabe Pharma, Nikkiso, Otsuka, TiGenix and Zambon. C Su, X Guo, I Modesto and R Mundayat are employees and shareholders of Pfizer Inc. DP Hudesman has received grants and personal fees from Pfizer Inc, and personal fees from AbbVie, Janssen, Salix and Takeda. MV Chiorean has received grants and personal fees from Takeda, and personal fees from AbbVie, Arena Pharmaceuticals, Celgene, Janssen, Medtronic, Pfizer Inc and Prometheus Laboratories.

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EFFICACY AND SAFETY OF TOFACITINIB RETREATMENT FOR ULCERATIVE COLITIS AFTER TREATMENT INTERRUPTION: AN UPDATE OF RESULTS FROM THE OCTAVE CLINICAL TRIALS

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis. Patients (pts) may need to temporarily suspend tofacitinib treatment for several reasons, such as adverse events (AEs), pregnancy or surgery; thus, it is key to assess the efficacy/safety of retreatment after treatment interruption.

Aims & Methods: We provide an update [1] of tofacitinib retreatment efficacy and safety data after treatment interruption in the ongoing, open-label, long-term extension (OLE) study (NCT01470612; data as of May 2019, database not locked). We analysed pts in the OLE study who had a clinical response after 8 wks of tofacitinib 10 mg twice daily (BID) in OCTAVE Induction 1&2 (NCT01465763; NCT01458951), then received placebo in OCTAVE Sustain (NCT01458574) and had treatment failure after Wk8 up to Wk52, and subsequently received tofacitinib 10 mg BID in the OLE study.

Treatment failure was defined as a ≥ 3 -point increase from OCTAVE Sustain baseline total Mayo score plus a ≥ 1 -point increase in rectal bleeding subscore and endoscopic subscore (ES) and an absolute ES ≥ 2 points after ≥ 8 wks of treatment. We evaluated efficacy up to Month 36 of the OLE study, and AEs throughout the study.

Results: Of 917 pts treated for ≥ 2 months in the OLE study, 100 entered the OLE study with a clinical response to tofacitinib 10 mg BID in OCTAVE Induction 1 or 2 followed by treatment failure on placebo during OCTAVE Sustain; median time to treatment failure was 135 days. After receiving tofacitinib 10 mg BID in the OLE study, clinical response was recaptured at Month 2 in 74.3% (non-responder imputation and last observation carried forward [NRI-LOCF]) and 85.2% of pts (observed data; Table). At Months 12, 24 and 36, 43.6%, 40.6% and 37.0% (NRI-LOCF) and 62.0%, 69.5% and

72.0% (observed data) of pts were in remission, respectively (Table). In pts with prior tumour necrosis factor inhibitor failure, 80.4% had a clinical response at Month 2 and 47.8%, 37.0% and 28.3% were in remission at Months 12, 24 and 36 (NRI-LOCF), respectively (Table). Corresponding observed data were 92.5%, 66.7%, 70.8% and 63.2%, respectively. Incidence rates for AEs are reported (Table).

	NRI-LOCF ^a		Observed case			
	All (N=101) ^b	Prior TNFi failure: Yes (N=46)	Prior TNFi failure: No (N=55)	All (N=100)	Prior TNFi failure: Yes (N=45)	Prior TNFi failure: No (N=55)
Clinical response,^c n/N (%)						
Month 2	75/101 (74.3)	37/46 (80.4)	38/55 (69.1)	75/88 (85.2)	37/40 (92.5)	38/48 (79.2)
Month 12	66/101 (65.3)	31/46 (67.4)	35/55 (63.6)	66/71 (93.0)	31/33 (93.9)	35/38 (92.1)
Month 24	55/101 (54.5)	23/46 (50.0)	32/55 (58.2)	55/59 (93.2)	23/24 (95.8)	32/35 (91.4)
Month 36	48/100 (48.0)	18/46 (39.1)	30/54 (55.6)	47/50 (94.0)	17/19 (89.5)	30/31 (96.8)
Remission,^d n/N (%)						
Month 2	40/101 (39.6)	21/46 (45.7)	19/55 (34.5)	40/88 (45.5)	21/40 (52.5)	19/48 (39.6)
Month 12	44/101 (43.6)	22/46 (47.8)	22/55 (40.0)	44/71 (62.0)	22/33 (66.7)	22/38 (57.9)
Month 24	41/101 (40.6)	17/46 (37.0)	24/55 (43.6)	41/59 (69.5)	17/24 (70.8)	24/35 (68.6)
Month 36	37/100 (37.0)	13/46 (28.3)	24/54 (44.4)	36/50 (72.0)	12/19 (63.2)	24/31 (77.4)
Safety						
	Retreatment (N=100) n (%); IR [95% CI]	Tofacitinib All, Nov 2017 (N=1157; 2050.5 PY) ^e n (%); IR [95% CI]				
Serious AEs	25 (25.0); 10.4 [6.7, 15.4]	189 (16.3); 9.5 [8.2, 11.0]				
SI ^f	7 (7.0); 2.7 [1.1, 5.6]	39 (3.4); 1.9 [1.3, 2.5]				
OI ^g	1 (1.0); 0.4 [0.0, 2.2]	25 (2.2); 1.2 [0.8, 1.8] ^h				
HZ ^h	6 (6.0); 2.4 [0.9, 5.3]	76 (6.6); 3.8 [3.0, 4.7]				
Malignancies ^{i,j}	3 (3.0); 1.2 [0.2, 3.4]	13 (1.2); 0.6 [0.3, 1.1] ^k				
NMSC ^l	1 (1.0); 0.4 [0.0, 2.2]	16 (1.4); 0.8 [0.4, 1.3] ^m				
MACE ⁿ	1 (1.0); 0.4 [0.0, 2.2]	6 (0.5); 0.3 [0.1, 0.6] ^o				
DVT	0 (0.0); 0.0 [0.0, 1.4]	0 (0.0); 0.0 [0.0, 0.2]				
PE	1 (1.0); 0.4 [0.0, 2.2]	4 (0.3); 0.2 [0.1, 0.5]				
Deaths	2 (2.0); 0.8 [0.1, 2.8]	5 (0.4); 0.2 [0.1, 0.6]				

Efficacy and safety data from subpopulations of FAS based on local read of endoscopy (data as of May 2019, database not locked). The retreatment subpopulation comprised pts who had a clinical response at Wk8 with tofacitinib 10 mg BID in OCTAVE Induction 1 or 2, and subsequent treatment failure with placebo during OCTAVE Sustain. Per protocol, these pts received tofacitinib 10 mg BID in the OLE study. ^aNRI-LOCF: non-responder imputation was applied after a pt discontinued and last observation carried forward imputation after a pt advanced to a subsequent study up to the visit they would have reached if they had stayed in the study. No imputation for missing data was applied for ongoing pts except non-responder imputation for intermittent missing data; ^bIncludes 1 pt who did not achieve a clinical response at Wk8 of OCTAVE Induction 1 or 2 and was enrolled into OCTAVE Sustain as a protocol deviation; ^cClinical response was defined as a decrease from induction study baseline total Mayo score of ≥ 3 points and $\geq 30\%$, plus a decrease in RB subscore of ≥ 1 point or an absolute RB subscore of 0 or 1; ^dRemission was defined as a total Mayo score of ≤ 2 with no individual subscore > 1 , and an RB subscore of 0; ^eAll pts who received tofacitinib 5 or 10 mg BID in Phase 2 and 3 trials (OCTAVE Induction 1&2, OCTAVE Sustain and OCTAVE Open), reported up to the Nov 2017 data cut-off (Sandborn WJ et al. J Crohns Colitis 2019;13(Suppl1):P466); ^fPer adjudication; ^gN=1124 (excludes Phase 2); ^hNon-serious and serious; ⁱExcludes NMSC; ^jAE, adverse event; BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; FAS, full analysis set; HZ, herpes zoster; IR, incidence rate (unique pts with events per 100 PY of exposure); MACE, major adverse cardiovascular events; N, number of evaluable pts; n, number of pts with response in the given category; NMSC, non-melanoma skin cancer; NRI-LOCF, non-responder imputation and last observation carried forward; OI, opportunistic infection; OLE, open-label, long-term extension; PE, pulmonary embolism; pts, patients; PY, pt-years; RB, rectal bleeding; SI, serious infection; TNFi, tumour necrosis factor inhibitor; Wk, Week

[Table. Summary of efficacy in the OLE study tofacitinib retreatment subpopulation (FAS)]

Conclusion: In this post hoc analysis, in pts with prior response to tofacitinib induction, retreatment with 10 mg BID after 8-52 wks of treatment interruption was efficacious and well-tolerated, with clinical response recaptured in the majority of pts by Month 2 and in half of pts at Month 36. The safety profile was generally consistent with that in the overall study population.

References: 1. Panés et al. J Crohns Colitis 2018;12(Suppl1):P516.

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SERUM LIPID AND C-REACTIVE PROTEIN LEVELS BY TREATMENT RESPONSE FOLLOWING 8 WEEKS OF TOFACITINIB INDUCTION THERAPY IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). Following 8 weeks of tofacitinib 10 mg twice daily (BID) in OCTAVE Induction 1&2, modest and reversible increases in serum lipid levels were reported in patients with UC, which were associated with reduced C-reactive protein (CRP) levels [1].

Aims & Methods: OCTAVE Induction 1&2 (NCT01465763; NCT01458951) were 2 identical, 8-week, Phase 3 studies in which patients with moderately to severely active UC received tofacitinib 10 mg BID or placebo (total N=1139).

In this post hoc analysis of the pooled induction studies, we assessed changes from baseline (CFB) in lipid levels (total cholesterol [total-c], high-density lipoprotein cholesterol [HDL-c], low-density lipoprotein cholesterol [LDL-c]) at Week 8 by responder and remitter status in patients who received tofacitinib 10 mg BID or placebo; analysis of variance was performed to estimate differences for responders or remitters vs non-responders. The association between CFB in lipid levels and CFB in CRP

levels (log-transformed), by responder and remitter status, was assessed using a linear regression model at Week 8 in patients who received tofacitinib 10 mg BID.

Results: Increases in lipid levels from baseline to Week 8 were observed in responders, non-responders and remitters (Table), which were greater with tofacitinib 10 mg BID vs placebo. There were significantly greater increases from baseline in total-c, HDL-c and LDL-c for responders vs non-responders (all $p < 0.0001$), and in total-c and HDL-c for remitters vs non-responders (both $p \leq 0.0001$) in patients who received tofacitinib 10 mg BID (Table). Significant differences in lipid levels by responder and remitter status were not reported with placebo (data not shown). In patients who received tofacitinib 10 mg BID, linear regression modelling showed a significant association between CFB in total-c, HDL-c and LDL-c and CFB in CRP in responders and non-responders, and between CFB in total-c and HDL-c and CFB in CRP in remitters (all $p < 0.01$) (Table).

Conclusion: These data suggest an association between increases in lipid levels and tofacitinib responder and remitter status. Further research is necessary to determine if increases in lipid levels can be used as a surrogate marker of reduced inflammation, and to establish lipid levels as potential predictors of patient outcomes to tofacitinib treatment.

Tofacitinib 10 mg BID		Estimated difference in CFB by responder and remitter status ^a (95% CI)		Association between CFB in lipid levels and CFB in CRP ^b estimated slopes of regression lines (95% CI)		Respon- ders vs non- responders		Remitters vs non- responders		Respon- ders		Non-re- sponders		Remitters	
	CFB at Week 8, mean (SE)														
Total-c, mg/dL	36.0 (1.4) ^a	21.6 (1.7) ^c	32.7 (2.6) ^a	-14.4 (-18.6, -10.2) $p < 0.0001$	-11.1 (-16.8, -5.4) $p < 0.0001$	-6.1 (-7.9, -4.3) ^a $p < 0.0001$	-6.0 (-8.3, -3.7) ^a $p < 0.0001$	-5.0 (-8.0, -2.0) ^a $p < 0.0011$							
HDL-c, mg/dL	15.4 (0.6) ^a	9.6 (0.7) ^c	15.4 (1.1) ^a	-5.8 (-7.6, -4.1) $p < 0.0001$	-5.9 (-8.3, -3.5) $p < 0.0001$	-3.1 (-3.9, -2.4) ^a $p < 0.0001$	-2.9 (-3.8, -2.0) ^a $p < 0.0001$	-3.6 (-4.9, -2.4) ^a $p < 0.0001$							
LDL-c, mg/dL	19.9 (1.2) ^a	12.4 (1.4) ^a	16.1 (2.1) ^a	-7.5 (-10.8, -4.1) $p < 0.0001$	-3.7 (-8.3, 0.9) $p = 0.1183$	-3.0 (-4.5, -1.6) ^a $p < 0.0001$	-2.6 (-4.6, -0.7) ^a $p = 0.0088$	-1.9 (0.5) $p = 0.1174$							
CRP, mg/L	-7.3 (0.7) ^a	-1.8 (1.2) ^c	-5.8 (1.1) ^a	N/R	N/R	N/A	N/A	N/A							

^aAnalysis of variance; ^bLinear regression model, CRP was log-transformed; ^cClinical response was defined as a decrease from induction study baseline total Mayo score of ≥ 3 points and $\geq 30\%$, plus a decrease in rectal bleeding subscore of ≥ 1 point or an absolute rectal bleeding subscore of 0 or 1; ^dRemission was defined as a total Mayo score of ≤ 2 with no individual subscore > 1 , and a rectal bleeding subscore of 0; ^eN=510; ^fN=317; ^gN=157; ^hN=508; ⁱN=316; ^jN=506; ^kN=314; ^lN=156; ^mN=504; ⁿN=158 BID, twice daily; CFB, change from baseline; CI, confidence interval; CRP, C-reactive protein; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; N, total number of evaluable patients per group; N/A, not applicable; N/R, not reported; SE, standard error; total-c, total cholesterol

[Table. Serum lipid and CRP levels by treatment response in patients who received tofacitinib 10 mg BID in the pooled OCTAVE Induction 1&2 studies]

References: 1. Sands et al. Clin Gastroenterol Hepatol 2020;18:123-32.e3.

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P0491

UPDATE ON LABORATORY PARAMETERS RELATED TO MONITORING IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH TOFACITINIB IN THE OCTAVE OPEN-LABEL, LONG-TERM EXTENSION STUDY

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). Changes in liver enzymes, lipids, haemoglobin (Hb), absolute neutrophil count (ANC) and absolute lymphocyte count (ALC) have been observed during 8-wk induction and 52-wk maintenance therapy with tofacitinib in patients (pts) with UC [1]. Monitoring of select parameters is recommended in pts treated with tofacitinib per product labelling [2].

Aims & Methods: Changes from baseline in liver enzymes, lipids, ANC, ALC and Hb were investigated in pts with UC treated with tofacitinib in an ongoing Phase 3, open-label, long-term extension (OLE) study (NCT01470612; data as of May 2019, database not locked). Pts who completed or demonstrated treatment failure in OCTAVE Sustain, or were non-responders after completing OCTAVE Induction 1 or 2, were eligible for the OLE study. Pts in remission at the end of OCTAVE Sustain received tofacitinib 5 mg twice daily (BID); all other pts received tofacitinib 10 mg BID in the OLE study.

Proportions of pts with laboratory values meeting protocol discontinuation criteria (Table), proportions of pts with investigator-defined treatment-emergent adverse events (TEAEs) of hyperlipidaemia, and proportions of pts with an addition of or change in lipid-lowering agent (LLA), were also evaluated.

Results: Changes from OLE study baseline in liver enzymes, lipids, ANC, ALC and Hb at Months 36 and 48, and the proportion of pts meeting protocol discontinuation criteria, are presented (Table). Findings were generally similar to the previously presented Sep 2018 data cut, which focused on Month 36 [3]. Hyperlipidaemia TEAEs occurred in 2.3% and 1.3% of pts treated with tofacitinib 5 and 10 mg BID, respectively.

Furthermore, 9.7% and 6.8% of pts treated with tofacitinib 5 and 10 mg BID, respectively, had a new LLA added, and 2.9% and 1.8% of pts treated with tofacitinib 5 and 10 mg BID, respectively, had their LLA dose increased.

Conclusion: No major changes from OLE study baseline were observed with tofacitinib in laboratory parameters recommended for monitoring up to Month 48. Proportions of pts meeting protocol discontinuation criteria

for liver enzymes, ANC, ALC or Hb, with hyperlipidaemia TEAEs, or with a change in LLA, were low. Due to OLE study dose assignment, pt baseline remission status differs across treatment arms.

Mean change from OLE study baseline in clinical laboratory parameters								
	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID		Month 36		Month 48	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Liver enzymes								
ALT, IU/L	117	3.68 (20.26)	47	2.34 (16.08)	310	7.66 (18.38)	189	8.96 (28.49)
AST, IU/L	117	3.46 (22.17)	47	-0.60 (9.36)	309	7.46 (14.70)	188	7.21 (12.14)
Lipids								
Cholesterol, mg/dL	121	-7.59 (38.08)	52	-14.10 (43.61)	328	20.60 (43.19)	213	16.87 (40.23)
HDL-c, mg/dL	121	-2.72 (9.75)	53	-4.13 (7.56)	328	6.45 (16.36)	213	5.06 (17.26)
LDL-c, mg/dL	119	-4.58 (34.99)	51	-10.97 (38.67)	326	12.00 (35.92)	213	9.82 (33.76)
LDL-c/HDL-c ratio	117	-0.02 (0.82)	51	-0.09 (0.74)	325	0.02 (0.67)	213	0.05 (0.72)
Triglycerides, mg/dL	120	-0.82 (63.79)	52	1.88 (81.33)	328	11.82 (60.82)	213	9.81 (57.61)
Haematology								
Hb, g/dL	117	0.29 (0.99)	49	-0.07 (1.15)	309	0.97 (1.63)	190	0.88 (1.61)
ALC, 10 ³ /mm ³	117	-0.20 (0.49)	49	-0.21 (0.58)	303	-0.52 (0.65)	187	-0.50 (0.65)
ANC, 10 ³ /mm ³	117	0.03 (1.78)	49	-0.34 (2.04)	303	-1.03 (2.34)	187	-1.27 (2.43)
Proportion of pts with laboratory values meeting protocol criteria for discontinuation, n/N (%)								
Liver enzymes ^a	1/175 (0.6) ^b	1/769 (0.1)						
ALC ^c	1/175 (0.6)	11/769 (1.4)						
ANC ^d	0/175 (0.0)	1/769 (0.1)						
Hb ^e	0/175 (0.0)	11/769 (1.4)						

Data as of May 2019, database not locked

All data are observed data

Tofacitinib dose was the starting dose in the OLE study

^aTwo sequential: AST or ALT elevations $\geq 3 \times$ ULN with ≥ 1 total bilirubin value $\geq 2 \times$ ULN; AST or ALT elevations $\geq 5 \times$ ULN; ^bOne pt met both of the liver enzyme protocol criteria for discontinuation; ^cTwo sequential ALC $< 500/\text{mm}^3$; ^dTwo sequential ANC $< 750/\text{mm}^3$; ^eTwo sequential Hb < 8.0 g/dL or $> 30\%$ decrease from baseline ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BID, twice daily; Hb, haemoglobin; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; N, number of pts with non-missing data; n, number of pts with event; OLE, open-label, long-term extension; pts, patients; SD, standard deviation; UC, ulcerative colitis; ULN, upper limit of normal

[Table. Change from baseline in clinical laboratory parameters, and proportion of pts with laboratory values meeting protocol discontinuation criteria]

References: 1. Sandborn et al. Clin Gastroenterol Hepatol 2019;17:1541-50. 2. EMA 2020. SmPC: Xeljanz. www.ema.europa.eu. 3. Melmed et al. UEG Journal 2019;7(Suppl):P0390.

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P0492

CLOSTRIDIUM DIFFICILE INFECTION IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH TOFACITINIB IN THE ULCERATIVE COLITIS PROGRAMME: AN UPDATE AS OF MAY 2019

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). Patients (pts) with UC are susceptible to *C. difficile* infection (CDI) [1]. In the tofacitinib UC clinical programme, previous analyses showed CDI rates among tofacitinib-treated pts to be similar or numerically lower than placebo (PBO)-treated pts and pts treated with immunomodulators and tumour necrosis factor inhibitors in a generally comparable claims-based observational cohort [2]. Here, we present an updated analysis of CDI in the tofacitinib UC clinical programme.

Aims & Methods: CDI events were evaluated from 4 randomised, PBO-controlled studies (Phase [P]2 and P3 induction studies [NCT00787202; NCT01465763; NCT01458951] and 1 maintenance P3 study [NCT01458574]) and an ongoing, open-label, long-term extension (OLE) study (NCT01470612). Three cohorts were analysed: Induction (P2/P3 induction studies), Maintenance (P3 maintenance study) and Overall (pts receiving tofacitinib 5 or 10 mg twice daily [BID] in P2, P3 or OLE studies; analysed by pts receiving ≥ 1 dose of tofacitinib and predominant dose [PD; 5 or 10 mg BID based on average daily dose < 15 mg or ≥ 15 mg, respectively]; data as of May 2019, database not locked). Proportions and incidence rates (unique pts with events per 100 pt-years [PY] of exposure) of CDI were evaluated. All pts underwent CDI screening; a positive test excluded pts from programme entry.

Results: The Overall Cohort comprised 1157 pts who received ≥ 1 dose of tofacitinib 5 or 10 mg BID, representing 2581 PY of tofacitinib exposure and up to 6.8 years of treatment. CDI occurred in 3 pts in the Induction Cohort (PBO, n=1; tofacitinib 10 mg BID, n=2), 3 pts in the Maintenance Cohort (PBO, n=3; CDI occurred 68, 81 and 98 days following initiation of PBO) and 9 pts in the Overall Cohort (PD tofacitinib 10 mg BID, n=9; Table). Overall Cohort pts with CDI were mild (n=4) or moderate (n=5) in severity; 6 pts continued study treatment without interruption, 1 temporarily discontinued and 2 permanently discontinued. CDI resolved with treatment in 8 pts, and CDI was still present in 1 pt at the time of study discontinuation. Two events were reported as serious adverse events due to hospitalisation.

Conclusion: In the tofacitinib UC programme, CDI rates among pts receiving tofacitinib have remained stable since the previous data cut [2] and are comparable to those reported for other advanced therapies [3].

	Induction Cohort (8 weeks) ^b	Maintenance Cohort (52 weeks) ^b	Overall Cohort (≤ 6.8 years) ^{b,c}					
	PBO (N=282; 44.8 PY)	Tofacitinib 10 mg BID (N=938; 156.2 PY)	PBO (N=198; 100.4 PY)	Tofacitinib 5 mg BID (N=198; 146.2 PY)	Tofacitinib 10 mg BID (N=196; 154.3 PY)	PD Tofacitinib 5 mg BID (N=198; 664.1 PY)	PD Tofacitinib 10 mg BID (N=959; 1917.1 PY)	Tofacitinib All (N=1157; 2581.3 PY)
Pts with CDI, n (%)	1 (0.4)	2 (0.2)	3 (1.5) ^e	0 (0.0)	0 (0.0)	0 (0.0)	9 (0.9)	9 (0.8) ^e
CDI IR (95% CI)	1.98 (0.05, 11.04)	1.21 (0.15, 4.35)	2.91 (0.60, 8.50)	0.00 (0.00, 2.48)	0.00 (0.00, 2.35)	0.00 (0.00, 0.54)	0.45 (0.21, 0.86)	0.34 (0.15, 0.64)

For Overall Cohort analysis, pts were categorised based on the average daily dose of tofacitinib (PBO exposure was not included): PD tofacitinib 5 mg BID (average total daily dose < 15 mg) and PD tofacitinib 10 mg BID (average total daily dose ≥ 15 mg)
^aPts with CDI were identified as those with an AE of CDI, *Clostridium difficile* colitis or *Clostridium difficile* test-positive, plus concomitant oral metronidazole, vancomycin or fidaxomicin (counted once per cohort); ^bExcluding events occurring after 28 days from the last dose of the corresponding cohort; ^cData as of May 2019, database not locked; ^dAll 3 pts received tofacitinib 10 mg BID during induction. CDI events occurred on Days 68, 81 and 98 following initiation of PBO in the maintenance study; ^eTwo pts had CDI events that met SAE reporting criteria; both were classified as SAEs due to hospitalisation AE, adverse event; BID, twice daily; CDI, *Clostridium difficile* infection; CI, confidence interval; IR, incidence rate (unique pts with events per 100 PY of exposure); N, number of pts; n, number of unique pts with CDI; PBO, placebo; PD, predominant dose; pts, patients; PY, pt-years; SAE, serious adverse event

[Table. Incidence rates of CDI^a among pts in the Induction, Maintenance and Overall Cohorts]

References: 1. Rahier et al. J Crohns Colitis 2014;8:443-68. 2. Loftus Jr. et al. Am J Gastroenterol 2019;114(Suppl):P035. 3. Ng et al. Inflamm Bowel Dis 2018;24:2431-41.

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P0493

PREGNANCY OUTCOMES IN THE TOFACITINIB ULCERATIVE COLITIS OCTAVE STUDIES: AN UPDATE AS OF FEBRUARY 2020

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Introduction: Pregnant women with ulcerative colitis (UC) have a higher risk of adverse pregnancy outcomes compared with age-matched controls [1]. Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of UC. In rats and rabbits, tofacitinib exhibits teratogenic effects at 146 and 13 times, respectively, the human dose of 5 mg twice daily. There are no adequately sized, well-controlled studies of tofacitinib in pregnant women.

Aims & Methods: We report updated pregnancy outcomes [2] from 3 randomised, placebo-controlled studies (OCTAVE Induction 1&2: NCT01465763, NCT01458951; OCTAVE Sustain: NCT01458574) and an ongoing, open-label, long-term extension study (OCTAVE Open: NCT01470612) of tofacitinib in patients (pts) with moderately to severely active UC [3,4]. Pregnancy outcomes following maternal or paternal exposure to tofacitinib were identified from Pfizer's internal safety database up to 11 Feb 2020, and categorised as healthy newborn, medical termination, foetal death, congenital malformation, spontaneous abortion or lost to follow-up. Trial protocols required females of childbearing potential to use highly effective contraception, and included regular urine β -hCG testing. The study drug was discontinued in pts who became pregnant.

Results: The UC OCTAVE trials included 1139 unique pts (including placebo), of whom 296 were females of childbearing age. A total of 34 pregnancies with exposure to tofacitinib were reported. Of these, 15 were cases of maternal exposure, all during the 1st trimester: 9 (60.0%) healthy newborns, 2 (13.3%) medical terminations, 2 (13.3%) spontaneous abortions and 2 (13.3%) cases lost to follow-up. There were 19 cases of paternal exposure: 15 (78.9%) healthy newborns, 2 (10.5%) spontaneous abortions and 2 (10.5%) cases lost to follow-up. There were no cases of foetal death or congenital malformation.

Conclusion: The majority of known outcomes for both maternal and paternal cases were healthy newborns. Although there are limited data and follow-up available, this analysis was consistent with a previous analysis in pts with UC [2], as well as an analysis in pts with rheumatoid arthritis and psoriasis [5]. Tofacitinib should not be used during pregnancy unless clearly necessary.

References: 1. Cornish et al. Gut 2007;56:830-7. 2. Mahadevan et al. UEG Journal 2017;5(Suppl):P0394. 3. Sandborn et al. N Engl J Med 2017;376:1723-36. 4. Lichtenstein et al. J Crohns Colitis 2020;14(Suppl1):DOP61. 5. Clowse et al. Drug Saf 2016;39:755-62.

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Prometheus Laboratories, and personal fees from Boehringer Ingelheim, Celgene, Eli Lilly, Genentech, Salix, Shire, Takeda and UCB. JK Yamamoto-Furusho has received grants and personal fees from Pfizer Inc and Takeda; grants from Bristol Myers-Squibb, Celgene and Shire; personal fees from AbbVie, Alfasigma, Almirall, Celltrion, Danone, Formosa, Ferring, Hospira, Janssen and UCB; and is a Past President of PANCCO. N Lawendy, TV Jones, N Kulisek, K Kwok and C Su are employees and shareholders of Pfizer Inc. GG Konijeti has received speakers' bureau fees from Takeda. HP Gröchenig has received lecture fees from AbbVie and Janssen.

	Foetal death ^a	Congenital malformation	Spontaneous abortion	Healthy newborn	Medical termination	Lost to follow-up
Maternal exposure (n=15)^a						
Tofacitinib 5 mg BID	0	0	1	1	0	0
Tofacitinib 10 mg BID	0	0	1	8 ^c	2 ^d	2
Paternal exposure (n=19)						
Tofacitinib 5 mg BID	0	0	1	5	0	0
Tofacitinib 10 mg BID	0	0	1	10 ^e	0	2

^aDefined as death after 20 weeks' gestation; ^bThe median maternal age at conception was 29 years (range 24-41 years); ^cIncluding 1 healthy newborn delivered preterm at 36 weeks; ^dCase 1: the patient decided to terminate pregnancy, based on the potential risks of tofacitinib; Case 2: reason unknown; ^eIncluding 1 healthy newborn delivered preterm at 34 weeks, and 2 healthy newborns from the same patient BID, twice daily

[Table. Summary of pregnancy outcomes in the OCTAVE programme]

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TOFACITINIB FOR THE TREATMENT OF ULCERATIVE COLITIS: UP TO 6.8 YEARS OF SAFETY DATA FROM GLOBAL CLINICAL TRIALS

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). Efficacy and safety of tofacitinib were evaluated in randomised, placebo-controlled Phase (P)2 (NCT00787202) and P3 (NCT01465763; NCT01458951; NCT01458574) studies, and in an ongoing, open-label, long-term extension (OLE) study (NCT01470612) [1-3]. We report updated tofacitinib safety analyses from the tofacitinib UC clinical programme, with exposure up to 6.8 years.

Aims & Methods: Two cohorts were analysed: P3 Maintenance (N=592; patients [pts] receiving placebo, tofacitinib 5 or 10 mg twice daily [BID]) and Overall (N=1157; pts receiving tofacitinib 5 or 10 mg BID in P2/P3/OLE

studies; data as of May 2019, database not locked). Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) were evaluated for adverse events (AEs) of special interest. Opportunistic infections (OIs), malignancies, major adverse cardiovascular events (MACE) and gastrointestinal (GI) perforations were reviewed by independent adjudication committees.

	Placebo (N=198; 100.4 PY)	Maintenance Cohort (52 weeks) Tofacitinib 5 mg BID (N=198; 146.2 PY)	Overall Cohort, Nov 2017 Tofacitinib 10 mg BID (N=196; 154.3 PY)	Overall Cohort, May 2019 Tofacitinib All (N=1157; 2050.5 PY)	Tofacitinib All (N=1157; 2581.3 PY)
Baseline demographics and clinical characteristics					
Age (years), mean (SD)	43.4 (14.0)	41.9 (13.7)	43.0 (14.4)	41.3 (13.9)	41.3 (13.9)
Total Mayo score, mean (SD)	3.3 (1.8)	3.3 (1.8)	3.4 (1.8)	8.6 (2.0)	8.6 (2.0)
Disease duration (years), mean (SD)	8.8 (7.5)	8.3 (7.2)	8.7 (7.0)	8.2 (7.0)	8.2 (7.0)
Prior TNFi failure, n (%)	89 (44.9)	83 (41.9)	92 (46.9)	583 (51.9)	583 (51.9)
AEs					
Pts with AEs, n (%)	149 (75.3)	143 (72.2)	156 (79.6)	969 (83.8)	980 (84.7)
Pts with SAEs, n (%)	13 (6.6)	10 (5.1)	11 (5.6)	189 (16.3)	210 (18.2)
Deaths					
n (%), IR [95% CI] ^a	0 (0.0), 0.00 [0.00, 3.57]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	5 (0.4), 0.24 [0.08, 0.55]	5 (0.4), ^b 0.19 [0.06, 0.44]
Infections					
n (%), IR [95% CI] ^a					
SIs ^d	2 (1.0), 1.94 [0.23, 7.00]	2 (1.0), 1.35 [0.16, 4.87]	1 (0.5), 0.64 [0.02, 3.54]	39 (3.4), 1.85 [1.32, 2.54]	45 (3.9), 1.70 [1.24, 2.27]
All HZ (non-serious and serious)	1 (0.5), 0.97 [0.02, 5.42]	3 (1.5), ^c 2.05 [0.42, 6.00]	10 (5.1), ^c 6.64 [3.19, 12.22]	76 (6.6), 3.79 [2.99, 4.74]	87 (7.5), 3.48 [2.79, 4.30]
OIs ^{e,g}	1 (0.5), 0.97 [0.02, 5.42]	2 (1.0), 1.36 [0.16, 4.92]	4 (2.0), 2.60 [0.71, 6.65]	25 (2.2), 1.20 [0.78, 1.78]	28 (2.5), 1.07 [0.71, 1.55]
Malignancies					
n (%), IR [95% CI] ^{a,f}					
Malignancies (excl. NMSC)	1 (0.5), ^h 0.97 [0.02, 5.39]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	13 (1.2), 0.62 [0.32, 1.06]	20 (1.8), ⁱ 0.75 [0.46, 1.16]
NMSC	1 (0.5), 0.97 [0.02, 5.40]	0 (0.0), 0.00 [0.00, 2.48]	3 (1.5), 1.91 [0.39, 5.59]	16 (1.4), 0.77 [0.44, 1.25]	19 (1.7), 0.73 [0.44, 1.13]
MACE	0 (0.0), 0.00 [0.00, 3.57]	1 (0.5), ^j 0.68 [0.02, 3.77]	1 (0.5), ^k 0.64 [0.02, 3.54]	6 (0.5), 0.29 [0.10, 0.62]	7 (0.6), ^l 0.26 [0.11, 0.54]
n (%), IR [95% CI] ^{a,f}					
VTE					
n (%), IR [95% CI] ^a					
DVT	1 (0.5), 0.97 [0.02, 5.39]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	0 (0.0), 0.00 [0.00, 0.17]	1 (0.1), ^m 0.04 [0.00, 0.21]
PE	1 (0.5), 0.98 [0.02, 5.44]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	4 (0.3), 0.19 [0.05, 0.48]	4 (0.3), ⁿ 0.15 [0.04, 0.38]
GI perforations	1 (0.5), 0.97 [0.02, 5.39]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	3 (0.3), 0.14 [0.03, 0.42]	3 (0.3), 0.11 [0.02, 0.33]
n (%), IR [95% CI] ^{a,o}					

Overall Cohort data as of Nov 2017 and May 2019, database not locked
^aFor the Maintenance Cohort, events that occurred >28 days after the last dose of study drug were excluded; for the Overall Cohort, all events, including those outside the 28-day risk period, were included; ^bDeaths (number of events): aortic dissection (1), PE (1), hepatic angiosarcoma (1), acute myeloid leukaemia (1), malignant melanoma (1); ^cEvents that occurred >28 days after the last dose of study drug were excluded; ^dDefined as any infection AE that requires hospitalisation or parenteral antimicrobials, or meets other criteria that require the infection to be classified as an SAE; ^eIRs of HZ in the Maintenance Cohort were numerically higher with tofacitinib 5 mg BID vs placebo and statistically higher with tofacitinib 10 mg BID vs placebo; ^fAdjudicated events; N=1124 (excludes Phase 2) for the Overall Cohort; ^gExcludes tuberculosis and HZ with 2 adjacent dermatomes; ^hInvasive ductal breast carcinoma; ⁱMalignancy (number of events): acute myeloid leukaemia (1), adenocarcinoma of colon (2), breast cancer (2), cervical dysplasia (2), cholangiocarcinoma (1), diffuse large B-cell lymphoma (1), Epstein-Barr virus associated lymphoma (1), essential thrombocythaemia (1), hepatic angiosarcoma (1), invasive ductal breast carcinoma (1), leiomyosarcoma (1), malignant melanoma (2), oesophageal adenocarcinoma (1), pulmonary mass (1), renal cell carcinoma (1), xerosis (1); ^jMyocardial infarction; ^kHaemorrhagic stroke; ^lMACE (number of events): acute coronary syndrome (1), acute myocardial infarction (1), aortic dissection (1), cerebellar haemorrhage (1), cerebrovascular accident (1), haemorrhagic stroke (1), myocardial infarction (1); ^mPt with DVT was diagnosed following a long-haul flight and management of an infected leg wound sustained in a recent motorbike accident; ⁿPts with PE had the following notable medical history: 1 with prior DVT and PE, 1 with phlebotrombosis and stroke, 1 was receiving oral contraceptives for dysfunctional uterine bleeding and 1 had cholangiocarcinoma and metastases to the peritoneum, and PE was the cause of death; ^oGI perforation excludes preferred terms of pilonidal cyst, perirectal abscess, rectal abscess, anal abscess, perineal abscess and any preferred terms containing the term fistula
 AE, adverse event; BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; GI, gastrointestinal; HZ, herpes zoster; IR, incidence rate (unique pts with events per 100 PY of exposure); MACE, major adverse cardiovascular events; N, number of pts treated in the treatment group; n, number of unique pts with a particular AE; NMSC, non-melanoma skin cancer; OI, opportunistic infection; PE, pulmonary embolism; pts, patients; PY, pt-years; SAE, serious AE; SD, standard deviation; SI, serious infection; TNFi, tumour necrosis factor inhibitor; UC, ulcerative colitis; VTE, venous thromboembolic events

[Table. Baseline demographics and disease characteristics, and IR for AEs of special interest in the tofacitinib UC clinical programme, for each cohort]

Results: Demographics, clinical characteristics and safety data are shown in the table. In the Overall Cohort, 1157 pts received ≥ 1 dose of tofacitinib 5 or 10 mg BID; most pts (N=959, 83%) received an average dose of 10 mg BID. Median treatment duration was 623 (range 1-2494) days (2581.3 PY of exposure). IRs (95% confidence intervals) for AEs of special interest were: deaths, 0.19 (0.06, 0.44); serious infections, 1.70 (1.24, 2.27); herpes zoster (non-serious and serious), 3.48 (2.79, 4.30); OIs, 1.07 (0.71, 1.55); malignancies (excl. non-melanoma skin cancer [NMSC]), 0.75 (0.46, 1.16); NMSC, 0.73 (0.44, 1.13); MACE, 0.26 (0.11, 0.54); deep vein thrombosis, 0.04 (0.00, 0.21); pulmonary embolism, 0.15 (0.04, 0.38); GI perforations, 0.11 (0.02, 0.33). Results in the Overall Cohort as per the previous Nov 2017 data cut are presented for context [4].

Conclusion: The safety profile of tofacitinib in pts with UC was manageable and consistent with that of other UC therapies, incl. biologics. Overall, IRs for AEs of interest have generally remained stable in the tofacitinib UC clinical programme over an extended period of time (up to 6.8 years).

References: 1. Sandborn et al. N Engl J Med 2012;367:616-24. 2. Sandborn et al. N Engl J Med 2017;376:1723-36. 3. Lichtenstein et al. J Crohns Colitis 2020;14(Suppl1):DOP61. 4. Sandborn et al. J Crohns Colitis 2019;13(Suppl1):P466.

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HERPES ZOSTER INFECTION IN PATIENTS WITH ULCERATIVE COLITIS RECEIVING TOFACITINIB: AN UPDATE AS OF MAY 2019

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). In a previous analysis, similar proportions of patients (pts) developed herpes zoster (HZ) with placebo and tofacitinib 10 mg twice daily (BID) during induction, whereas HZ events were higher for tofacitinib 5 or 10 mg BID vs placebo during maintenance [1]. We present an update on HZ in the tofacitinib UC clinical programme, as of May 2019.

Aims & Methods: HZ incidence rates (IRs; unique pts with events per 100 pt-years of exposure) were evaluated in a Phase (P)2 induction study (NCT00787202), 2 P3 induction studies (NCT01465763; NCT01458951), a P3 maintenance study (NCT01458574) and an ongoing, open-label, long-term extension (OLE) study (NCT01470612). Three cohorts were analysed: Induction (P2 and P3 induction studies), Maintenance (P3 maintenance study) and Overall (all pts receiving tofacitinib 5 or 10 mg BID in P2/P3/OLE studies [data as of May 2019, database not locked]; ≤ 6.8 years of treatment). Cox regression was used for risk factor analysis. No pre-treatment HZ vaccination was required.

Results: HZ IRs are shown in the table. Overall Cohort HZ (non-serious and serious) IR was 3.48 (95% confidence interval [CI] 2.79, 4.30). Of all HZ, > 90% were mild/moderate in severity, > 90% were resolved at data cut-off and > 90% were non-serious. Eight (9.2%) pts with HZ permanently discontinued. HZ was limited to 1-2 dermatomes in 63 (5.4%) pts, multidermatomal in 17 (1.5%) pts, and disseminated in 7 (0.6%) pts (Table); 4 (4.6%) pts had post-herpetic neuralgia. Older age (hazard ratio [95% CI] 1.40 [1.21, 1.63]; p < 0.0001), lower body weight (1.02 [1.01, 1.04]; p < 0.01), North American vs European region (2.14 [1.28, 3.59]; p < 0.05) and prior tumour necrosis factor inhibitor failure (1.76 [1.13, 2.74]; p < 0.05) were HZ risk factors. Although not significant in the multivariate model, pts of Asian race had higher HZ risk vs non-Asian pts (univariate model; 1.84 [1.11, 3.06]; p = 0.0187). Baseline steroid use was not a significant risk factor.

Conclusion: HZ is a known risk with tofacitinib treatment. In the Maintenance Cohort, HZ IR was numerically higher with tofacitinib 10 vs 5 mg BID. Over time in the Overall Cohort, IRs were similar between doses

and remained stable vs the previous data cut [1]. Most HZ was non-serious, limited to 1-2 dermatomes. As shown here and in the general population, elderly pts had increased HZ risk. Further study of HZ risk mitigation is warranted for pts with UC receiving tofacitinib.

	Induction Cohort (8 weeks) ^a	Maintenance Cohort (52 weeks) ^a	Overall Cohort (≤6.8 years) ^a	Overall Cohort, Dec 2016 (≤4.4 years) ^{a,b}			
	Placebo (N=282; 44.8 PY)	Tofacitinib 10 mg BID (N=938; 156.2 PY)	Placebo (N=198; 100.4 PY)	Tofacitinib 5 mg BID (N=198; 146.2 PY)	Tofacitinib 10 mg BID (N=196; 154.3 PY)	Tofacitinib All (N=1157; 2581.3 PY)	Tofacitinib All (N=1157; 1612.8 PY)
Age (years), mean (SD)	41.4 (14.4)	41.3 (13.8)	43.4 (14.0)	41.9 (13.7)	43.0 (14.4)	41.3 (13.9)	41.3 (13.9)
Total Mayo score at baseline, mean (SD)	8.9 (1.5)	9.0 (1.5)	3.3 (1.8)	3.3 (1.8)	3.4 (1.8)	8.6 (2.0)	8.6 (2.0)
Treatment duration (days), mean (SD) [range]	57.9 (13.7) [7-80]	60.8 (11.0) [1-96]	185.1 (127.9) [14-382]	269.7 (125.1) [22-420]	287.4 (123.1) [1-399]	814.8 (706.0) [1-2494]	509.1 (389.8) [1-1606]
HZ^c							
n (%)	1 (0.4)	6 (0.6)	1 (0.5)	3 (1.5)	10 (5.1)	87 (7.5)	65 (5.6)
IR	1.98	3.62	0.97	2.05	6.64	3.48 ^d	4.07
[95% CI]	[0.05, 11.05]	[1.33, 7.88]	[0.02, 5.42]	[0.42, 6.00]	[3.19, 12.22]	[2.79, 4.30]	[3.14, 5.19]
HZ multi-dermatomal^{e,f}							
n (%)	0 (0.0)	1 (0.1)	1 (0.5)	1 (0.5)	4 (2.0)	17 (1.5)	11 (1.0)
IR	0.00	0.63	0.97	0.68	2.60	0.65	0.67
[95% CI]	[0.00, 9.13] ^g	[0.02, 3.51] ^h	[0.02, 5.42]	[0.02, 3.77]	[0.71, 6.65]	[0.38, 1.04] ⁱ	[0.33, 1.20]
HZ disseminated^j							
n (%)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.5)	0 (0.0)	7 (0.6)	6 (0.5)
IR	0.00	0.63	0.00	0.68	0.00	0.26	0.36
[95% CI]	[0.00, 9.13] ^g	[0.02, 3.51] ^h	[0.00, 3.57]	[0.02, 3.77]	[0.00, 2.35]	[0.11, 0.54] ^k	[0.13, 0.79]

Overall Cohort data are as of May 2019, database not locked

^aAs per the SCS analysis convention, only events occurring within 28 days after the last dose are included in this table for calculation of proportion and IR; ^bAs per data cut-off Dec 2016, database not locked; Winthrop et al. J Crohns Colitis 2018;12(Suppl1):P512; ^cNon-serious and serious;

^dOverall Cohort HZ IRs [95% CI] were 3.41 [2.11, 5.22] for PD tofacitinib 5 mg BID and 3.50 [2.71, 4.46] for PD tofacitinib 10 mg BID; ^eMultidermatomal HZ = non-adjacent dermatomes or >2 adjacent dermatomes; ^fConfirmed by independent adjudication; ^gN=234; ^hN=905; ⁱN=1124; ^jDisseminated HZ = any of: diffuse rash >6 dermatomes, HZ meningitis (encephalitis), other non-skin organ involvement;

^kOther organ involvement: keratitis (1), ophthalmic HZ (1), HZ meningitis (encephalitis) (1) BID, twice daily; CI, confidence interval; HZ, herpes zoster; IR, incidence rate (unique pts with events per 100 PY of exposure); N, number of pts treated in the treatment group; n, number of unique pts with HZ infection;

PD, predominant dose; pts, patients; PY, pt-years; SCS, summary of clinical safety; SD, standard deviation

[Table. Demographics and proportions and IRs (unique pts with events per 100 PY) for HZ events for the Induction, Maintenance and Overall Cohorts]

References: 1. Winthrop et al. J Crohns Colitis 2018;12(Suppl1):P512.

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TOFACITINIB FOR THE TREATMENT OF ULCERATIVE COLITIS:
AN UPDATED ANALYSIS OF INFECTION RATES IN THE
TOFACITINIB ULCERATIVE COLITIS CLINICAL PROGRAMME

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). We present updated infections data from the tofacitinib UC clinical programme [1], as of May 2019.

Aims & Methods: Infection events were evaluated in a Phase (P)2 induction study (NCT00787202), 2 P3 induction studies (NCT01465763; NCT01458951), a P3 maintenance study (NCT01458574) and an ongoing, open-label, long-term extension (OLE) study (NCT01470612) as 3 cohorts: Induction (P2 and P3; placebo [PBO] or tofacitinib 10 mg twice daily [BID]),

Maintenance (P3; PBO, tofacitinib 5 or 10 mg BID) and Overall (all patients [pts] receiving tofacitinib 5 or 10 mg BID in P2/P3/OLE studies; by predominant dose [5 or 10 mg BID based on average daily dose < 15 mg or ≥ 15 mg, respectively]; as of May 2019, database not locked). Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure; censored at time of event) were evaluated for infections, serious infections (SIs), opportunistic infections (OIs; independently adjudicated, incl. non-herpes zoster [HZ] OIs) and HZ.

Results: 1157 pts received ≥ 1 dose of tofacitinib 5 or 10 mg BID (83% predominantly 10 mg BID), with 2581.3 PY of exposure (up to 6.8 years). Nasopharyngitis was the most frequent infection in the Overall Cohort (251 pts; 21.7%). In induction, SIs and OIs were numerically higher with tofacitinib vs PBO (Table). The Overall Cohort SI IR was 1.70, which was generally similar to Maintenance Cohort IRs for tofacitinib 5 and 10 mg BID and PBO, and the Overall Cohort IR (1.75) in the previous report. No SIs resulted in death. OIs were infrequent (28 pts; IR 1.07), and most OIs were HZ (24 pts; IR 0.92; mostly cutaneous). Overall, 87 pts had HZ (non-serious and serious; IR 3.48 [95% confidence interval (CI) 2.79, 4.30]); 7 serious. Maintenance Cohort HZ IR was numerically higher for tofacitinib 10 vs 5 mg BID, but with overlapping 95% CIs; Overall Cohort HZ IRs were similar between doses.

Conclusion: Overall, SIs were generally infrequent, and similar (indirectly) to other UC therapies, incl. biologics [2]. In induction, SIs and OIs were more frequent with tofacitinib vs PBO. In the Maintenance Cohort, HZ IR was numerically higher with tofacitinib 10 vs 5 mg BID. Over time in the Overall Cohort, IRs were similar between doses and remained stable vs the previous data cut [1]. Non-HZ OIs and viral infections were rare.

	Induction Cohort (8 weeks) ^a	Maintenance Cohort (52 weeks) ^a	Overall Cohort (≤6.8 years) ^a	Overall Cohort, Sep 2018 (≤6.1 years) ^{a,b}					
	PBO (N=282; 44.8 PY)	Tofacitinib 10 mg BID (N=938; 156.2 PY)	PBO (N=198; 100.4 PY)	Tofacitinib 5 mg BID (N=198; 146.2 PY)	Tofacitinib 10 mg BID (N=196; 154.3 PY)	PD Tofacitinib 5 mg BID (N=198; 664.1 PY)	PD Tofacitinib 10 mg BID (N=959; 1917.1 PY)	Tofacitinib All (N=1157; 2581.3 PY)	Tofacitinib All (N=1157; 2403.6 PY)
Infections (all)									
n (%)	43 (15.2)	196 (20.9)	48 (24.2)	71 (35.9)	78 (39.8)	132 (66.7)	506 (52.8)	638 (55.1)	629 (54.4)
IR [95% CI]	93.23 [67.47, 125.57]	134.25 [116.11, 154.42]	58.16 [42.88, 77.12]	62.54 [48.85, 78.89]	72.82 [57.56, 90.88]	43.38 [36.30, 51.45]	52.57 [48.09, 57.36]	50.37 [46.53, 54.43]	51.90 [47.92, 56.12]
SIs^c									
n (%)	0 (0)	8 (0.9)	2 (1.0)	2 (1.0)	1 (0.5)	8 (4.0)	37 (3.9)	45 (3.9)	43 (3.7)
IR [95% CI]	0.00 [0.00, 7.30]	4.83 [2.09, 9.52]	1.94 [0.23, 7.00]	1.35 [0.16, 4.87]	0.64 [0.02, 3.54]	1.18 [0.51, 2.33]	1.87 [1.32, 2.58]	1.70 [1.24, 2.27]	1.75 [1.27, 2.36]
OIs^d									
n (%)	0 (0)	3 (0.3)	1 (0.5)	2 (1.0)	4 (2.0)	8 (4.0)	20 (2.2)	28 (2.5) ^e	28 (2.5) ^e
IR [95% CI]	0.00 [0.00, 9.13]	1.89 [0.39, 5.53]	0.97 [0.02, 5.42]	1.36 [0.16, 4.92]	2.60 [0.71, 6.65]	1.23 [0.53, 2.42]	1.02 [0.62, 1.58]	1.07 [0.71, 1.55]	1.16 [0.77, 1.67]
Non-HZ OIs^{d,f}									
n (%)	0 (0)	1 (0.1)	0 (0)	0 (0)	0 (0)	1 (0.5)	3 (0.3)	4 (0.4)	4 (0.4)
IR [95% CI]	0.00 [0.00, 9.13]	0.63 [0.02, 3.51]	0.00 [0.00, 3.57]	0.00 [0.00, 2.48]	0.00 [0.00, 2.35]	0.15 [0.00, 0.82]	0.15 [0.03, 0.44]	0.15 [0.04, 0.38]	0.16 [0.04, 0.42]
All HZ^g									
n (%)	1 (0.4)	6 (0.6)	1 (0.5)	3 (1.5)	10 (5.1)	21 (10.6)	66 (6.9)	87 (7.5)	83 (7.2)
IR [95% CI]	1.98 [0.05, 11.05]	3.62 [1.33, 7.88]	0.97 [0.02, 5.42]	2.05 [0.42, 6.00]	6.64 [3.19, 12.22]	3.41 [2.11, 5.22]	3.50 [2.71, 4.46]	3.48 [2.79, 4.30]	3.57 [2.84, 4.43]

Overall Cohort data are as of May 2019, database not locked. For the Overall Cohort, pts were categorised based on the average daily dose of tofacitinib (PBO exposure was not included); PD tofacitinib 5 mg BID (average total daily dose <15 mg) and PD tofacitinib 10 mg BID (average total daily dose ≥15 mg)

^aOnly pts with events occurring within 28 days after the last dose are included in this table for calculation of proportion and IR; ^bAs per data cut-off Sep 2018, database not locked; Winthrop et al. UEG Journal 2019;7(Suppl):OP007;

^cInfections meeting serious AE reporting criteria (any AE that results in death, persistent or significant disability/incapacity or congenital anomaly/birth defect, is life-threatening, or requires immediate hospitalisation or prolongation of existing hospitalisation); ^dOIs were adjudicated by an independent committee; calculated as percentage (%), based on the number of pts in the studies in which adjudication was performed; excludes P2 pts; ^eOf the 28 patients with OIs in the Overall Cohort: HZ (24) (HZ OIs were either multidermatome [2 non-adjacent or 3-6 adjacent dermatomes; 17 patients] or disseminated [any of: diffuse rash >6 dermatomes, HZ meningitis (encephalitis), other non-skin organ involvement; 7 patients]; other organ involvement: keratitis (1), ophthalmic HZ (1), HZ meningitis (encephalitis) (1)), CMV infection (1), histoplasmosis (1), CMV hepatitis (1), pulmonary mycosis (1); Non-HZ OIs included CMV hepatitis (1), CMV colitis (1; based on a colonic biopsy showing a positive polymerase chain reaction test for CMV), histoplasmosis (1; with pulmonary involvement) and pulmonary mycosis (1; cryptococcosis); there were no events of new EBV infection reported; 1 event of lymphoma in an EBV-positive pt was reported; ^fNon-serious and serious; 4 pts with HZ had post-herpetic neuralgia AE, adverse event; BID, twice daily; CI, confidence interval; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HZ, herpes zoster; IR, incidence rate (unique pts with events per 100 PY of exposure); N, number of pts treated in the treatment group; n, number of unique pts with a particular AE; OI, opportunistic infection; P, Phase; PBO, placebo; PD, predominant dose; pts, patients; PY, pt-years; SI, serious infection

[P0496 Table. Summary of incidence of treatment-emergent infections (all causality) in the Induction, Maintenance and Overall Cohorts]

References: 1. Winthrop et al. UEG Journal 2019;7(Suppl):OP007. 2. Shah et al. Inflamm Bowel Dis 2017;23:570-7.

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P0497

PROACTIVE THERAPEUTIC DRUG MONITORING IN THE EARLY PHASE OF INFLIXIMAB THERAPY: RESULTS FROM A 30 WEEK MULTICENTRE RANDOMISED TRIAL OF 400 PATIENTS (THE NOR-DRUM STUDY)

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Introduction: Therapeutic drug monitoring (TDM), an individualised treatment based on assessments of serum drug levels, has been proposed to optimise efficacy and safety of infliximab (IFX) and other tumor necrosis factor inhibitors (TNFi) used for immune mediated inflammatory diseases.

To date, no clinical trial has shown that TDM improves clinical outcomes. NOR-DRUM is the first randomised trial to evaluate proactive TDM in the induction phase of TNFi treatment.

Aims & Methods: In the investigator-initiated, randomised, open-label, multicentre NOR-DRUM study, adult patients with ulcerative colitis (n=83), Crohn's disease (n=58), rheumatoid arthritis (n=84), psoriatic arthritis (n=45), spondyloarthritis (n=119), and psoriasis (n=22) starting IFX therapy were randomly assigned to dosage of IFX based on TDM (TDM arm) or to standard dosage of IFX (control arm). In the TDM arm, the dose and interval were adjusted according to IFX trough levels guided by an interactive eCRF to have the therapeutic target level >20 µg/ml at infusion 2, >15 µg/ml at infusion 3 and in the range 3-8 µg/ml thereafter. The aim of the study was to assess if proactive TDM was superior to standard treatment in order to achieve clinical remission in the early phase of IFX treatment. The primary endpoint was clinical remission at week 30 based on disease specific indices, analysed by mixed effect logistic regression in the full analyses set, adjusting for diagnoses.

Results: Between March 1, 2017 and January 10, 2019, 411 patients from 21 study centres starting IFX therapy were randomised in the NOR-DRUM trial. In total 398 (198 in the TDM group and 200 in the control group) were exposed to the algorithm and included in the primary analyses. The two groups were well balanced at baseline regarding disease duration and activity, previous biological therapy and usage of concomitant immunosuppressives. Clinical remission at week 30 was present in 100 (53%) and 106 (54%) of patients in the TDM and control arm, respectively (adjusted difference 1.5%; 95% confidence interval (CI), -8.2, 11.1) (table). There were no differences between the study groups across diseases (table). Likewise, consistent results were shown across arms regarding time to remission and sustained remission, level of serum IFX, C-reactive protein, erythrocyte sedimentation rate, and patient reported outcome measures. The number and type of adverse events did not differ between groups, infections were most frequent event. However, infusion reactions were less frequent in the TDM arm (5 (2.5%) vs. 16 patients (8.0%), difference 5.5%; 95% CI 1.1, 9.8). Thirty-six patients (18%) in the TDM group and 34 (17%) in the control group developed anti-drug antibodies (≥15 µg/L). Of these, the proportion of patients in clinical remission at week 30 was numerically higher in the TDM-group (20/36 (56%)) than in the control group (12/34 (35%)).

Conclusion: Proactive TDM in the early phase of IFX treatment did not improve clinical outcomes in the NOR-DRUM study. However, fewer infusion reactions in the TDM group indicate improved safety.

	TDM group (n=198)	Control group (n=200)	Difference in remission rate (95% CI)
Overall	100/189 (52.9%)	106/196 (54.1%)	1.5% (-8.2, 11.1)
Ulcerative Colitis	25/38 (65.8%)	29/41 (70.7%)	4.9% (-15.6, 25.5)
Crohn's Disease	17/28 (60.7%)	17/26 (65.4%)	4.7% (-21.1, 30.4)
Rheumatoid Arthritis	21/36 (58.3%)	21/42 (50.0%)	-8.3% (-30.4, 13.8)
Psoriatic Arthritis	5/18 (27.8%)	12/21 (57.1%)	29.4% (-0.2, 59.0)
Spondyloarthritis	23/57 (40.4%)	21/57 (36.8%)	-3.5% (-21.4, 14.4)
Psoriasis	9/12 (75.0%)	6/9 (66.7%)	-8.3% (-47.7, 31.0)

[Difference in clinical remission rate at week 30, overall and by disease]

Disclosure: KKJ reports personal fees from Intercept, Norgine, AOP Orphan Pharmaceuticals and Celltrion.

P0498

AN UPDATE ON THE ANALYSIS OF NON-MELANOMA SKIN CANCER IN THE TOFACITINIB ULCERATIVE COLITIS CLINICAL PROGRAMME AS OF MAY 2019

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). We present an updated [1] analysis of non-melanoma skin cancer (NMSC) events in the tofacitinib UC clinical programme as of May 2019.

Aims & Methods: NMSC events were evaluated from 3 randomised, placebo-controlled studies (2 Phase [P]3 induction studies [NCT01465763; NCT01458951] and 1 maintenance P3 study [NCT01458574]) and an ongoing, open-label, long-term extension (OLE) study (NCT01470612). Three cohorts were analysed: Induction (P3 induction studies), Maintenance (P3 maintenance study) and Overall (patients [pts] receiving tofacitinib 5 or 10 mg twice daily [BID] in P3 or OLE studies). Analysis was by predominant dose (PD) 5 or 10 mg BID, based on average daily dose < 15 mg or ≥ 15 mg, respectively (82.4% of pts assigned PD 10 mg BID). An independent adjudication committee reviewed potential NMSC. Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) were evaluated for NMSC. A Cox proportional hazards model was used for risk factor analysis.

Results: 1124 pts were evaluated for NMSC (2576.4 PY of tofacitinib exposure; ≤ 6.8 years of treatment). NMSC events in the Induction and Maintenance Cohorts were previously reported (Table) [1]. NMSC occurred in 19 Overall Cohort pts (IR 0.73 [95% confidence interval (CI) 0.44, 1.13]; PD tofacitinib 5 mg BID, n=3, IR 0.45 [0.09, 1.30]; PD tofacitinib 10 mg BID, n=16, IR 0.82 [0.47, 1.34]) (Table); no new cases since Sep 2018 [1]. No NMSC was metastatic or led to discontinuation. Prior NMSC (hazard ratio [HR] 9.09 [95% CI 2.98, 27.73]), prior tumour necrosis factor inhibitor (TNFi) failure (HR 3.32 [1.08, 10.20]) and age (per 10-year increase, HR 2.03 [1.37, 3.02]) were significant risk factors for NMSC.

Conclusion: NMSC events were infrequent with tofacitinib treatment and more likely to occur in pts with prior NMSC, prior TNFi failure and with increasing age - known NMSC risk factors [2]. Dose dependency of NMSC IR could not be concluded here, as dose changes were permitted. NMSC IRs were similar to those previously reported in the tofacitinib UC clinical programme [1] and in pts with UC treated with biologics [3].

References: 1. Lichtenstein et al. UEG Journal 2019;7(Suppl):P0393. 2. Marcil, Stern. Arch Dermatol 2000;136:1524-30. 3. FDA Advisory Committee Meeting sNDA 203214. FDA 2018:S18.

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All NMSC	Induction Cohort (8 weeks) ^a	Maintenance Cohort (52 weeks) ^a	Overall Cohort (≤6.8 years)			
	Placebo (N=234; 38.2 PY)	Tofacitinib 10 mg BID (N=905; 151.2 PY)	Placebo (N=198; 100.4 PY)	Tofacitinib 5 mg BID (N=198; 146.2 PY)	Tofacitinib 10 mg BID (N=196; 154.3 PY)	Tofacitinib All (N=1124; 2576.4 PY)
Age (years), mean (SD)	41.4 (14.4)	41.2 (13.8)	43.4 (14.0)	41.9 (13.7)	43.0 (14.4)	41.2 (13.9)
NMSC, n (%)	0 (0.0),	2 (0.2),	1 (0.5),	0 (0.0),	3 (1.5),	19 (1.7),
IR	0.00	1.26	0.97	0.00	1.91	0.73
[95% CI]	[0.00, 9.13]	[0.15, 4.56]	[0.02, 5.40]	[0.00, 2.48]	[0.39, 5.59]	[0.44, 1.13] ^b
Overall Cohort, Tofacitinib All (N=1124)						
Univariate subgroup analysis	N	n (%)	IR [95% CI]			
Age, years	≥50	315	15 (4.8)	1.78 [1.00, 2.94]		
	40-50	241	4 (1.7)	0.68 [0.19, 1.74]		
	30-40	304	0 (0.0)	0.00 [0.00, 0.54]		
	<30	264	0 (0.0)	0.00 [0.00, 0.72]		
Prior TNFi treatment	Yes	612	15 (2.5)	1.15 [0.64, 1.89]		
	No	512	4 (0.8)	0.31 [0.08, 0.78]		
Prior immunosuppressant treatment	Yes	838	18 (2.1)	0.93 [0.55, 1.46]		
	No	286	1 (0.3)	0.15 [0.00, 0.83]		

Overall Cohort data as of May 2019, database not locked

^aAs per the SCS analysis convention, only events occurring within 28 days after the last dose are included in this table for calculation of proportion and IR; ^bIncluding 5 pts from the P3 Induction and Maintenance Cohorts; 7 pts had prior NMSC history; 16 pts had received PD tofacitinib 10 mg BID (average total daily dose ≥15 mg; IR 0.82; 95% CI 0.47, 1.34) and 3 had received PD tofacitinib 5 mg BID (average total daily dose <15 mg; IR 0.45; 95% CI 0.09, 1.30). In the Overall Cohort, the majority (84.2%) of pts with NMSC were receiving the PD 10 mg BID dose; however, due to the design of the OCTAVE studies, the majority (926/1124; 82.4%) of pts received PD tofacitinib 10 mg BID. Ten pts had SCC and 14 pts had BCC; 5 pts had both SCC and BCC. BCC, basal cell carcinoma; BID, twice daily; CI, confidence interval; IR, incidence rate (unique pts with events per 100 PY of exposure); N, number of pts treated in the treatment group; n, number of pts in a specified category; NMSC, non-melanoma skin cancer; P, Phase; PD, predominant dose; pts, patients; PY, pt-years; SCC, squamous cell carcinoma; SCS, summary of clinical safety; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

[Table. Demographics, and proportions and IRs for all NMSC events, in the Induction, Maintenance and Overall Cohorts]

P0499

OVERCOMING SECONDARY LOSS OF RESPONSE TO INFLIXIMAB IN PATIENTS WITH ULCERATIVE COLITIS WITH THE USE OF MESENCHYMAL STROMAL CELLS OF THE BONE MARROW

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Introduction: Long-term experience with infliximab (IFX) shows that within a year, 20-30% of patients with ulcerative colitis (UC) develop acquired drug resistance (secondary inefficiency).

Aims & Methods: To establish the possibility of overcoming the secondary inefficiency of IFX in UC patients using mesenchymal stromal cells (MSC). Materials and methods. In the IBD treatment Department, the clinical status of 84 UC patients receiving IFX therapy was evaluated. Secondary loss of response was registered in 28 UC patients, which required optimization of IFX therapy. 12 patients (group 1), in order to overcome the secondary loss of response, were administered MSCS three times every 4 weeks, 16 patients with UC (group 2) received standard optimized IFX therapy. The effectiveness of therapy was evaluated after 12 weeks of therapy (reduction of the Mayo score) and normalization of laboratory parameters (ESR, C-reactive protein (CRP), hemoglobin, fecal calprotectin (FCP). The comparative analysis was carried out using the method of four-field tables using nonparametric statistical criteria.

Results: In 10 (83.3%) of 12 patients of group 1, a significant positive dynamics was observed after 12 weeks: a decrease in the Mayo index and normalization of laboratory parameters (ESR, CRP, hemoglobin, FCP). In 4 (25.0%) patients with UC from group 2, against the background of optimized IFX therapy, a significant positive dynamics was also observed with a decrease in the Mayo index and an improvement in ESR, CRP, hemoglobin and FCP levels. However, 12 patients from group 2 were transferred to therapy with other anti-TNF- α drugs and drugs with a different mechanism of action (HR-0.222, 95% CI 0.061-0.812; χ^2 - 7.146; $p=0.00334$).

Conclusion: The use of mesenchymal stromal cells of the bone marrow contribute to overcome the secondary loss of response to infliximab in patients with ulcerative colitis.

Disclosure: Nothing to disclose

P0500

SAFETY AND EFFICACY OF USTEKINUMAB FOR CROHN'S DISEASE (CD): THE CROSS PENNINE EXPERIENCE

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Introduction: Ustekinumab was approved by NICE in 2016 for adults with moderate to severe CD. Real world data are required to establish effectiveness of therapy where restrictive inclusion and exclusion criteria from trials are not routinely applied.

Aims & Methods: This retrospective audit of clinical data included all patients treated with Ustekinumab for CD at 8 North West England and Yorkshire hospitals that form the Cross Pennine IBD Initiative. The dataset included medical history, treatment history, phenotype and disease activity (at 3 and 12 months). Remission was defined as Physician Global Assessment (PGA) of 0 and response by PGA of 1.

Results: The cohort comprised of 259 patients (160 females, mean age 39.99, mean disease duration 11.78 years) with active Crohn's Disease. The majority (n=137) had ileocolonic, 65 colonic and 57 ileal disease distribution. Eighty six (33.2%) had inflammatory, 78 (30.1%) stricturing and 95 (36.7%) penetrating disease behaviour. Perianal disease was noted in 32.1% and 46% had had a previous bowel resection. Previous treatment history included Infliximab in 73%, Adalimumab in 80.7% and Vedolizumab in 30.1% with 35.5% having been exposed to 1, 40.5% to 2 and 22.4% to 3 previous biologics. Steroid exposure at baseline was 36.7%.

At 3 months 89 (34.4%) had achieved remission and 84 (32.4%) had a clinical response. By 12 months 65 (25%) patients had discontinued Ustekinumab, 63 (24.3%) were in remission and 34 (13.1%) in response (outcomes not available for 37.6%). Bowel resections were required in 20 and perianal surgery in 6 cases. 84% of patients were given 8-weekly sc ustekinumab.

Adverse events included headaches (8), joint pains/arthritis (8), body rashes/urticaria (6) and flu type symptoms (5). Serious adverse events included hospitalisations with infection (17), gastrointestinal operations (26), CD flare (46), abdominal pain (6), medical admissions (8). There was one death from a pre-existing primary malignant melanoma, 3 cases of newly diagnosed cancers (1 small bowel adenocarcinoma, 1 breast cancer, 1 hepatocellular carcinoma), and 2 recurrences of previous known cancers (1 basal cell carcinoma of the skin, 1 bladder transitional cell carcinoma).

Conclusion: In this large real-world study of patients with long disease duration and highly refractory CD we found that Ustekinumab was clinically effective and safe in line with expectations from clinical trials. Further analysis of predictors of response may help clinicians' decision making on biologic choices for CD.

Disclosure: The study was supported by a grant from Janssen.

P0501

NO BENEFIT OF CONCOMITANT IMMUNOMODULATOR THERAPY ON EFFICACY OF NON - ANTI-TNF BIOLOGICS IN INFLAMMATORY BOWEL DISEASES: A META-ANALYSIS

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Introduction: There is debate over whether patients with inflammatory bowel diseases treated with non-anti-TNF biologics should receive concomitant immunomodulators. We conducted a meta-analysis to compare the efficacy and safety of concomitant immunomodulator therapy vs vedolizumab/ustekinumab monotherapy.

Aims & Methods: In a systematic search of publications, through July 31, 2019, we identified

31 studies (randomized controlled trial, n=6 ; cohort studies, n= 25) of patients with IBD treated with vedolizumab or ustekinumab. The primary outcome measure was the clinical benefit including clinical remission or clinical response in IBD patients with combination therapy as compared to those who were not. Secondary outcome measures were endoscopic improvement, and safety. We performed random-effects meta-analysis and estimated odds ratio (OR) and 95% CIs.

Results: Overall, combination therapy was not associated with better clinical outcomes for both vedolizumab (15 studies - OR 0.88; 95% CI 0.81-1.10 - I2 = 6%, Q test-p=0.22) and ustekinumab (13 studies - OR 1.1; 95% CI 0.87-1.40 - I2 = 12%, Q test-p=0.330). Results were consistent in subgroup analysis with no difference in terms of clinical benefit in induction and maintenance studies, and in both Crohn's disease and ulcerative colitis for vedolizumab. Combination therapy was not associated with better endoscopic outcomes for both vedolizumab (2 studies - OR 1.11; 95% CI 0.43-2.88 - I2= 0%, Q test-p=0.889) and ustekinumab (2 studies - OR 0.58 95% CI, 0.21-1.16 - I2= 47%, Q test-p=0.17). Combination therapy was not associated with an increase in adverse events during vedolizumab therapy (4 studies - OR 1.17; 95% CI 0.75-1.84 - I2 = 0%, Q test-p=0.110).

Conclusion: On the basis of a meta-analysis, combination therapy of vedolizumab or ustekinumab with an immunomodulator is no more effective than monotherapy as induction or maintenance therapy.

Disclosure: Nothing to disclose

P0502

TREATMENT PATTERNS OF COMPLEX PERIANAL FISTULA IN CROHN'S DISEASE IN BELGIUM, FRANCE, GERMANY, ITALY AND SPAIN: THE PREFACE STUDY, A RETROSPECTIVE CHART REVIEW

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Introduction: Presence of fistulas in Crohn's disease (CD) is an indicator of poor prognosis; 20% of CD patients suffer from perianal fistula¹. There is limited information available about the management of complex perianal fistula (CPF) in a real-world setting. This study describes the treatment patterns of patients with CPF in CD in Europe.

Aims & Methods: Retrospective medical chart review including consecutive patients with CD receiving treatment for a new episode of CPF during the eligibility period (September 2011 to September 2014), in Belgium, France, Germany, Italy and Spain. Index date was defined as the date of treatment initiation for a new episode of CPF during the eligibility period. Data was collected from CD diagnosis to at least 3 years after index date (except for deceased or lost to follow-up patients) to describe patient characteristics and treatments used for all CPFs episodes since CD diagnosis.

Results: A total of 372 patients (49% female) were included from 31 sites with a mean (SD) age of 37.8 (13.1) at index date and a mean (SD) of 9.9 (8.9) years since CD diagnosis. At CD diagnosis, 27% of patients had ileal, 28% colonic and 39% ileocolonic involvement. One fourth (25%) of study patients had anal or perianal fistula at diagnosis. Prior to index date, 41% of patients had at least one surgery for CD and complications being partial resection of small bowel the most common one. 5-ASA, anti-TNFs and immunosuppressants were used for CD, complications and CPFs for 48%, 46% and 42% of patients, respectively. Patients presented a total of 564 CPFs from CD diagnosis until end of observational period. The following results are based on the 498 CPFs at index date and during the post-index period to focus on more current treatment patterns. More than half of these CPFs were trans-sphincteric (61%). Out of the 498 CPFs, 94% were treated with at least one surgical intervention (most frequent: 57% long-term seton placement, 48% surgical drainage), and 81.5% with at least one medical treatment. Medical treatments most frequently used for CPFs or CD and complications (overlapping a CPF episode) were antibiotics (43%), anti-TNFs (40%) and immunosuppressants (14%).

Conclusion: One fourth of the patients with CPF already had anal or perianal fistulas at CD diagnosis. Based on ECCO guidelines, it was expected that the vast majority of all CPFs in CD patients should be treated with anti-TNF with or without surgical intervention.

However, the use of anti-TNF during CPF episodes was lower than expected. The reason for this was not covered by this study. Future researches on this topic might be necessary for a better understanding. Surgical drainage and seton placement were performed in a majority of patients within

3 years following treatment intensification, with a low rate for other types of surgery. Almost two third of CPFs were trans-sphincteric and if inadequately treated, sphincter function may be compromised.

References: 1. Schwartz DA et al. The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. *Gastroenterology* 2002 Apr; 122(4):875-80.

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P0503

REAL-WORLD EXPOSURE-RESPONSE RELATIONSHIP OF VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE: A POOLED MULTICENTRE OBSERVATIONAL COHORT ANALYSIS OF CLINICAL AND MODELED PHARMACOLOGICAL DATA

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Introduction: The role of therapeutic drug monitoring of vedolizumab (VDZ) in patients with ulcerative colitis (UC) or Crohn's disease (CD) is under investigation. However, a thorough understanding of the relationship between VDZ concentrations and clinical outcomes is lacking.

Aims & Methods: ERELATE was a retrospective cohort study conducted at 9 tertiary centres in 6 countries. Data were pooled from real-world clinical cohorts of patients with UC or CD treated with intravenous VDZ. Clinical, endoscopic and biologic remission outcomes based on commonly used definitions across centres were collected at Weeks 14, 26 and 52. Using a population pharmacokinetic model,¹ VDZ dosing, baseline body weight and albumin concentration were used to predict VDZ serum concentra-

tions. A Bayesian approach incorporated observed VDZ concentrations to refine individual predicted concentrations. Relationships between predicted concentrations and observed clinical and deep remission (clinical and endoscopic or biologic remission) were investigated. VDZ concentration thresholds were determined using the optimal Youden index point along the receiver operating characteristic curve.

Correlation and agreement between observed and predicted concentrations were evaluated using Spearman (ρ) and intra-class correlation (ICC) coefficients, respectively. Observed data were analysed; patients who discontinued VDZ because of no response to induction or loss of response during maintenance therapy were considered treatment failures for subsequent timepoints.

Results: In total 695 patients (304 UC, 391 CD) were included; 47.9% were male. Median age was 39 years, median disease duration was 9 years and 86.3% had prior anti-tumour necrosis factor exposure. For UC, at Weeks 14, 26 and 52, rates of clinical remission were 55.2%, 52.3% and 39.8%; endoscopic remission were 59.7%, 50.9% and 42.4%; deep remission were 41.7%, 30.6% and 23.7%, respectively. For CD, at Weeks 14, 26 and 52, rates of clinical remission were 41.8%, 43.4% and 31.7%; endoscopic remission were 65.6%, 69.8% and 68.6%; deep remission were 23.5%, 30.1% and 20.9%. Significant correlation ($[p=0.879; p<0.01]$ across all timepoints) and agreement (ICC=0.722; $p<0.01$) were noted between observed and predicted concentrations, indicating adequate Bayesian model prediction of individual VDZ concentrations. An exposure-response relationship was observed and was more pronounced in UC than CD.

Differences in VDZ concentrations and area under the curve of drug concentration from Weeks 0-6 were observed between remitters and non-remitters for UC and CD combined (Table). Predicted VDZ concentrations of 30.8 and 33.8 $\mu\text{g/mL}$ at Week 6 and 16.6 and 14.4 $\mu\text{g/mL}$ at Week 14 were associated with clinical remission and deep remission, respectively, at Week 52.

	Clinical Remission W14	Clinical Remission W52	Deep Remission W14	Deep Remission W52				
Predicted vedolizumab trough concentration in UC and CD	Yes (N=215)	No (N=236)	Yes (N=126)	No (N=233)	Yes (N=120)	No (N=265)	Yes (N=66)	No (N=236)
W6 Median, $\mu\text{g/mL}$	34.1	29.5	32.9	29.2	36.5	29.3	36.6	29.0
W6 Threshold, $\mu\text{g/mL}$	29.9**	30.8**	29.8**	33.8**				
W10 Median, $\mu\text{g/mL}$	34.8	30.5	35.3	30.3	37.5	30.3	39.3	30.1
W10 Threshold, $\mu\text{g/mL}$	30.5**	32.5**	33.4**	27.5**				
W14 Median, $\mu\text{g/mL}$	19.6	16.2	17.5	15.6	22.9	16.9	18.9	15.6
W14 Threshold, $\mu\text{g/mL}$	21.3**	16.6*	20.1**	14.4*				
Difference in AUC of drug concentration W0-6* (95% CI), % ^b	5.0* (1.1, 8.4)	5.9* (0.5, 9.6)	10.4** (6.5, 16.8)	11.6** (5.2, 19.2)				

Analyses were conducted in the exposure-response relationship set, which included patients incorporated into the pharmacokinetic model, using the non-responder imputation method.

Predicted concentration thresholds were delineated with an area under receiver operating characteristic curve ranging between 0.577-0.699.

P-values associated with thresholds represent significance of area under the receiver operating characteristic curve from 0.5; p-values associated with AUC represent a comparison of the median AUCs between patients in remission and those not in remission.

AUC, area under the curve; CD, Crohn's disease; CI, confidence interval; UC, ulcerative colitis; W, week.

*Cumulative AUC from W0 to W6, including all vedolizumab doses received from W0 to W6.

^bRatio (%) and 95% CIs were calculated by dividing median difference (95% CI) by median of non-remitters.

* $p<0.05$; ** $p<0.01$

[Table. Predicted Vedolizumab Trough Concentrations Associated With Clinical and Deep Remission in Patients With UC or CD]

Conclusion: These real-world data confirm GEMINI trial findings of significant relationships between VDZ serum concentration and clinical outcomes. Adequate drug concentrations during induction therapy may be important predictors of short- and long-term treatment outcomes.

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support: Janssen, Takeda, Abbvie, Celltrion. ID: Consultant/advisory board member for: Pfizer, Abbvie, Janssen, Takeda, Genentech, Neopharm, Celltrion, Celgene, Arena, Gilead, Medtronic/given imaging, Rafa Laboratories, DSM; Speaker for: Takeda, Abbvie, Janssen, Genentech, Pfizer, Ferring, Falk Pharma, Celltrion, Nestle, Celgene/BMS; Research support from: Pfizer, Abbvie, Altman Research. MO: Financial support for research from UCB; Consultancy fees from: Abbvie, Elan, Janssen, Lycera, Merck, Pfizer, Takeda, UCB, DL: Employee of Takeda; holds Takeda stock or stock options. CA: Employee of Takeda; holds Takeda stock or stock options. MR: Employee of Takeda at the time this research was conducted; has granted patents and pending patent applications relating to the clinical pharmacology of vedolizumab. TO: Employee of Takeda; holds Takeda stock or stock options.

P0504

EARLY DETECTION OF ANTI-DRUG-ANTIBODIES USING DRUG-TOLERANT ASSAY WITHIN THE INDUCTION PHASE AT WEEK 2 PREDICTS THE LOSS OF CLINICAL RESPONSE TO ANTI-TNF IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Several studies investigated the relationships between circulating anti-TNF levels during induction therapy and disease outcomes in inflammatory bowel disease (IBD). Few data on the early occurrence of anti-drug antibodies at induction phase are available.

Aims & Methods: **Aims:** to investigate whether early detection of anti-Adalimumab antibodies (AAA) or anti-Infliximab antibodies (ATI) during the induction phase of anti-TNF therapy was predictive of time-to-treatment discontinuation and also to determine the optimal threshold of anti-drug antibodies.

Patients and methods: In a prospective, observational study, all consecutive IBD patients who should start anti-TNF therapy were enrolled and followed prospectively every 3 months for adalimumab (ADA) treated patients and at each infliximab (IFX) infusion for the others over a 24-month period or earlier in case of loss of response (LOR) or adverse events requiring treatment discontinuation. During induction therapy, anti-TNF trough levels and antidrug antibodies were measured at W2 and W6 using a drug tolerant assay. Time to treatment discontinuation was determined using Kaplan Meier survival analysis and the best threshold of antidrug antibodies for predicting time of treatment discontinuation at 9, 12, 18 and 24 months was identified using receiver operating characteristic (ROC) curves.

Results: One hundred and eight IBD patients were enrolled, including 54 patients starting ADA (mean age: 36 years, sex ratio M/F=1.16, CD: 65%) and 54 starting IFX (mean age: 35 years, sex ratio M/F=0.86, CD: 59%). At W2, AAA (> 2.0 µg/ml eq) and ATI (≥ 4µg/ml eq) were detected in 75.9% and 53.7% of patients under ADA and IFX, respectively. Time to treatment discontinuation was significantly shorter in presence of AAA or ATI at W2 in patients under ADA or IFX compared with that in absence (6 months vs 24 months, respectively (HR=18.51; 95CI=4.35-78.11; p<0.001) and (5.5 months vs >24 months, respectively (HR=13.89; 95CI=4.08-47.31; p<0.001), respectively). An AAA threshold level >2.0 µg/ml-eq under ADA and an ATI threshold level ≥4µg/ml-eq under IFX were predictive of treatment failure

within 24 months with a sensitivity of 78.8% and 61.988.0%, respectively and a specificity of 100% for both. In multivariate analysis, AAA ($> 2.0 \mu\text{g/ml}$ eq) or ATI ($\geq 4 \mu\text{g/ml}$ eq) at W2 was the only independent factor associated with treatment failure (HR=18.57; 95CI: 4.27-77.45; $p<0.001$ and HR=13.37; 95CI: 3.89-45.92; $p<0.001$, respectively for ADA and IFX therapies).

Conclusion: The prevalence of anti-drug antibody in IBD patients treated with anti-TNF is very high (more than three quarter of them under ADA and more than half under IFX) when detected early and when using a drug-tolerant assay. Early detection of AAA and ATI was the only independent predictor of further treatment discontinuation in IBD patients under ADA and IFX.

References: 1- Ben horin S et al GUT 2011

Disclosure: X Roblin served as a speaker, a consultant and/or an advisory board member for MSD, Pfizer, Janssen, Takeda, Abbvie, Amgen, Biogen, Gilead, Roche, Gilead, Theradiag P Veyrard served as a speaker, a consultant and/or an advisory board member for MSD, Pfizer, Janssen, Takeda, Abbvie, Amgen Q Tournier None declared S Paul served as a speaker, a consultant and/or an advisory board member for MSD, Abbvie, Pfizer, Theradiag N Williet None declared E Berger None declared JM Phelip None declared B Le Roy none declared S Nancey served as a speaker, a consultant and/or an advisory board member for MSD, Pfizer, Janssen, Takeda, Abbvie, Amgen, Biogen, Roche, Novartis G Boschetti served as a speaker, a consultant and/or an advisory board member for Abbvie, Pfizer, Takeda, Ferring, Amgen, MSD, Mayoly, Hospira. B Flourie served as a speaker, a consultant and/or an advisory board member for MSD, Abbvie, Amgen, Ferring, Norgine, Biocodex

P0505

IN FAILURE OF NON-OPTIMIZED ADALIMUMAB (ADA) WITH THERAPEUTIC SERUM LEVELS, A CHANGE IN BIOTHERAPY CLASS IS GREATER THAN AN INTENSIFICATION OF ADA DOSE IN PATIENTS WITH CROHN'S DISEASE AND HEMORRHAGIC RECTOCOLITIS

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Introduction: Nearly 40% of patients who failed on ADA have therapeutic residual trough levels (pharmacodynamic failure). It is then recommended to change the therapeutic class to a non-anti-TNF biological. In this situation, however, a quarter of patients respond to an ADA dose optimization. Thus, it is not yet clear whether a class change is more favorable than a dose optimization in patients with IBD in pharmacodynamic failure under ADA.

Aims & Methods: The purpose of this work was to compare these two strategies and identify predictors of response for each strategy.

Subjects and method: This is a bi-center, retrospective study based on a clinical and biological database that included patients followed from 2014 to 2016 with an IBD in maintenance treatment with ADA as monotherapy (40mg/sc/14 days) and in loss of response (CDAI > 220 with fecal calprotectin $> 250 \mu\text{g/g}$ stool for CD and Mayo score > 6 with endoscopic sub-score > 1 for UC). All patients included had residual trough ADA levels $> 5 \mu\text{g/ml}$. Relapsed patients were treated either with dose optimization (ADA: 40mg/sc/7 days) or other biotherapy (ustekinumab, UST Temporary Recommen-

dation or vedolizumab, VEDO according to WMA regimens and dosages). The primary endpoint was the relapse-free survival rate (defined as clinical and biological or endoscopic activity requiring therapeutic change). The survival curve analysis was performed using the Kaplan-Meier method and the Log-Rank test. A uni- and then multivariate analysis looked for predictive factors for relapse.

Results: 125 patients (mean age: 38 years, 75% CD, sex ratio M/F=57%, previous infliximab = 42%) were included and 50 were treated with another biological (Vedolizumab: 30 patients, Ustekinumab: 20 patients). The characteristics of the two groups were comparable except for significantly higher levels of CRP and fecal calprotectin at inclusion in the biological change arm. The duration without relapse was significantly longer after class change ($p=0.0005$; HR=0.39[0.23-0.68]). The relapse-free survival rates at 54 weeks were 35% for the optimized arm and 66% for a class change ($p=0.04$). In multivariate analysis, the only long-term response predictor was biotherapy class change versus ADA dose optimization ($p=0.042$; HR=0.3[0.02-0.95]). Previous use of IFX or the type of IBD were not associated with relapse. For the dose optimization strategy, in multivariate analysis, only age < 40 years was associated with a progression without relapse ($p=0.007$; HR=0.09[0.01 - 0.52]). Residual ADA levels were not predictive of response to optimization ($p=0.73$) and no ADA quartile was significantly associated with a favorable clinical response. For the class change strategy, no relapse predictors were isolated in univariate analysis.

Conclusion: In patients on ADA who are losing response despite therapeutic rates, the change of class to non-anti-TNF biotherapy allows a significantly greater lasting response than a dose optimization strategy for ADA. However, more than one in three patients responded to optimization without the ADA rates before it being predictive of the outcome. Thus, an optimization could be proposed initially, followed by a change of class in case of failure without pejorative or severe disease.

Disclosure: XR : MSD, Janssen, Takeda, Pfizer, Abbvie, Biogen, Amgen, Theradiag

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Introduction: Large post-marketing data are required to confirm the effectiveness and safety of UST in CD in clinical practice.

Aims & Methods: Our aims were: to assess UST short-term effectiveness, durability of the response to UST in the long-term and to evaluate the safety of UST in clinical practice. Retrospective, multicentre study (>60 sites). Patients with active CD [Harvey-Bradshaw (HBI) >4] that received at least 1 dose of UST intravenously before July 2018 were included. Clinical remission was defined as HBI score ≤4, and clinical response as a decrease in HBI ≥3 points. Loss of efficacy was defined as reappearance of symptoms that led to intensify the treatment dose, add another medication to control CD, switching or surgery in patients with short-term remission. Short-term response was evaluated at week 8 and after the induction (week 16).

Factors associated with short-term remission were assessed by multivariate analysis. The cumulative incidence of loss of efficacy was evaluated by survival curves, and predictive factors were assessed by Cox-regression. Adverse events (AE) were recorded. Data quality was assured by remote monitoring.

Results: 463 CD patients were included: median age was 45 years, median disease duration 11 years, 26 were smokers, 47% had abdominal surgery, 47% ileocolonic location, 28% structuring and 19% penetrating behavior, 72% had been exposed to 1-2 biologics and 24% to ≥3 biologics. Median HBI at baseline was 8, and 35% received concomitant immunomodulators (IMM). At week 8, 58% of patients responded (44% had remission). At week 16, 70% of patients responded (56% had remission). Similar data were obtained in patients receiving UST according to SmPC (68% response; 55% remission) In the multivariate analysis, older age [Odds ratio (OR)=0.6, 95%CI=0.4-0.9], previous surgery (OR=0.6 95%CI=0.4-0.9) and higher HBI at baseline (OR=0.8, 95%CI=0.8-0.9) were associated with lower probability of achieving remission at week 16.

With respect to response to UST, previous surgery was the only factor associated with a lower probability of having response at week 16 (OR=0.7, 95%CI=0.4-1). 256 patients were in remission at week 16; 89 (35%) lost response (LoR) over time (median follow-up 9.6 months). The probability of maintaining remission was 78% at 6, 66% at 12 and 56% at 18 months. The incidence rate of LoR was 42% per-patient year of follow-up; the number of previous biologics [Hazard ratio (HR)=1.2, 95%CI=1-1.5 and higher HBI

score at baseline [moderate vs. mild (HR=1.5, 95%CI=1-2.3) and severe vs. mild (HR=4, 95%CI=1-17)] were associated with higher risk of LoR. Concomitant treatment with IMM showed no benefit on long-term response. After LoR, 13 patients escalated the dose (from every 12 to every 8 weeks) and 67 intensified the dose (interval administration below 6 weeks); 69% of patients that escalated the dose and 58% of those who intensified the dose regained response. Incidence rate of UST discontinuation due to LoR among those in remission after induction was 12% per patient-year of follow-up. 50 AE were reported in 39 (8.4%) patients, only 4 of them were severe (2 infections, 1 neoplasia and 1 fever).

Conclusion: SustAIN is the largest real clinical practice study of UST to treat CD patients with the longest follow-up reported to date. UST was demonstrated to be effective in real world use even in a highly refractory cohort. A proportion of patients lost benefit over time but dosage adjustment was able to recapture response in 58% of them. Safety was consistent with the known profile of UST.

References: *Equal contributors as senior authors

Disclosure: Nothing to disclose

P0507

LONG-TERM DURABILITY AND SAFETY OF USTEKINUMAB (UST) IN PATIENTS WITH ACTIVE CROHN'S DISEASE (CD) IN REAL LIFE: SUSTAIN STUDY

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Introduction: Large post-marketing studies are required to confirm the durability, long-term benefit and safety of UST in CD in clinical practice. SustAIN is the largest real clinical practice study of UST to treat CD patients with the longest follow-up reported to date.

Aims & Methods: Our aims were to evaluate the retention rate of UST in CD patients, to identify predictive factors of UST discontinuation and to evaluate UST safety in clinical practice. Retrospective, multicentre study (>60 sites). Patients with active CD [(Harvey-Bradshaw (HBI) >4)] receiving ≥1 dose of UST intravenously (IV) before July 2018 were included. Clinical remission and response were defined according to HBI. Loss of efficacy was defined as reappearance of symptoms that led to intensify treatment dose, add another medication to control CD, switching or surgery in patients with short-term remission. Dose escalation was defined as shortening UST intervals from every-12-weeks to every-8-weeks; dose de-escalation as an increase from every-8-weeks to every-12-weeks; in-

tensification as shortening intervals below every-6-weeks. Retention rate was evaluated by survival curves, and predictive factors were assessed by Cox-regression. Adverse events (AE) were recorded. Data quality was assured by remote monitoring.

Results: 463 CD patients were included: 47% had abdominal surgery, 72% had been exposed to 1-2 biologics and 24% to ≥ 3 biologics. Median HBI at baseline was 8 and 35% received concomitant immunomodulators (IMM). 91% of patients started maintenance with UST administration every-8-weeks. 107 (23%) patients discontinued UST treatment during a median 15 months of follow-up. Incidence rate of discontinuation was 18% per patient-year of follow-up. The probability of maintaining UST treatment was 91% at 6, 83% at 12, 76% at 18 and 73% at 24 months. Similar data were obtained for patients receiving UST according to SmPC (88%, 79%, 72% and 67% at 6, 12, 18 and 24 months).

Reasons for discontinuation were: primary non-response (23%), loss of response (LoR) (22%), partial response (13%), AE (6%), patients' choice (5.6%) and others (30%). In the multivariate analysis, previous abdominal surgery [Hazard ratio (HR)=2.2, 95% confidence interval (CI)=1.5-3.5] and concomitant steroids (HR=1.7, 95%CI=1.1-2.5) were associated with higher risk of UST discontinuation, while UST administration every-12-weeks (vs. every-8-weeks) was associated with lower risk of UST discontinuation (HR=0.2, 95%CI=0.1-0.8).

Neither the concomitant treatment with IMM nor the number of previous biologics was associated with UST persistence. 27 patients (6%) de-escalated treatment, 25 of them due to sustained remission 9 of whom needed to escalate treatment again mainly (78%) due to LoR. A total of 21 (4.5%) patients escalated the treatment during follow-up mainly due to LoR (62%) and primary failure (24%); 80% of escalated patients responded to the dosage change and, 25% of them lost response over time again. 100 patients (22%) intensified the treatment, being the main reasons LoR (71%) and primary failure (17%); 70% responded and, of them, 28% lost response over time. 6 patients received reinduction with an IV dose and 83% regained response (one of them relapsed). 50 AE were reported in 39 (8.4%) patients, only 4 of them were severe (2 infections, 1 neoplasia and 1 fever).

Conclusion: Over 80% of patients maintained UST treatment at 1 year, even in a highly refractory CD cohort, primary failure being the main reason for UST discontinuation. Dosage adjustments are feasible to maintain UST benefit over time.

References: *Equal contributors as senior authors

Disclosure: Nothing to disclose

P0508

PHYSICIAN PREFERENCES FOR BIOLOGICS FOR THE TREATMENT OF CROHN'S DISEASE AND ULCERATIVE COLITIS IN FRANCE, GERMANY AND THE UNITED KINGDOM

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Introduction: Biologics are well established as effective treatment options for patients with Crohn's disease (CD) and ulcerative colitis (UC). Biologics can be costly and access may be limited; less expensive biosimilars have thus been developed and approved to treat and manage symptoms. Real-world CD and UC prescribing patterns and treatment preferences are not yet well understood in this new treatment landscape.

Aims & Methods: The aim of this retrospective study was to characterize physician preferences for biologics for the treatment of CD and UC in France, Germany and the UK. As part of a broader chart review study, physician panel vendor Medefield collected treatment preferences from gastroenterologists and general practitioners (GPs) who had treated ≥ 10 patients (aged ≥ 18 years) with a diagnosis of moderate-to-severe CD or UC and who had received ≥ 1 CD- or UC-related biologic any time from 1 January 2014 to 18 November 2019. Descriptive statistics were used to describe the sample by disease type, physician specialty and treatment preference.

Results: Overall, 348 physicians (267 [76.7%] gastroenterologists; 81 [23.3%] GPs) were included from France (33.0%), Germany (41.1%) and the UK (25.9%). Physicians contributed a total of 425 patients with CD (mean [SD] age 37.0 [12.7] years; 54.6% men) and 593 patients with UC (38.7 [12.9] years; 63.4% men); 14 patients had both.

For first-line treatment of CD and UC, physicians generally preferred anti-TNFs over other treatments; originator anti-TNFs were selected more than their biosimilars (CD: 69.5% vs 30.5%; UC: 73.9% vs 26.1%). A higher percentage of physicians preferred the adalimumab originator (CD: 30.2%; UC: 26.7%) than its biosimilars (CD: 14.1%; UC: 8.9%); the same was true for infliximab (CD: 31.6% vs 16.4%; UC: 39.1% vs 17.2%). Adalimumab and infliximab biosimilars were selected more often by gastroenterologists than GPs (CD: 38.2% vs 5.0%; UC: 33.0% vs 3.7%; Table 1).

Efficacy was the most commonly reported reason for treatment preference among physicians who preferred originators (CD: 93.4%; UC: 94.6%) and biosimilars (CD: 88.7%; UC: 87.9%). Physicians who preferred biosimilars cited affordability or availability as reasons for preference (CD: 37.7%; UC: 42.9%) more often than those who preferred originators (CD 14.9%; UC: 11.3%).

For second-line treatment in patients with CD in whom anti-TNF therapy failed, GPs preferred vedolizumab over ustekinumab (54.3% vs 30.9%), though gastroenterologists had no strong preference (49.8% and 50.2%, respectively). In patients with UC, both gastroenterologists and GPs preferred vedolizumab over tofacitinib (85.0% vs 15.0% and 66.7% vs 18.5%, respectively).

First treatment preference, n (%)	Crohn's disease	Ulcerative colitis		
	Gastroenterologists (n = 267)	General practitioners (n = 81)	Gastroenterologists (n = 267)	General practitioners (n = 81)
Adalimumab originator	70 (26.2)	35 (43.2)	61 (22.8)	32 (39.5)
Biosimilars of adalimumab	47 (17.6)	2 (2.5)	29 (10.9)	2 (2.5)
Infliximab originator	78 (29.2)	32 (39.5)	95 (35.6)	41 (50.6)
Biosimilars of infliximab	55 (20.6)	2 (2.5)	59 (22.1)	1 (1.2)
Ustekinumab	8 (3.0)	8 (9.9)	-	-
Vedolizumab	9 (3.4)	2 (2.5)	13 (4.9)	1 (1.2)
Golimumab	-	-	10 (3.7)	3 (3.7)
Tofacitinib	-	-	0 (0.0)	1 (1.2)

[First-line anti-TNF treatment preferences in patients with Crohn's disease and ulcerative colitis]

Conclusion: Anti-TNF originator biologics are generally preferred by physicians for treating patients with moderate-to-severe CD and UC in the three European countries studied. This is primarily driven by efficacy; however, preferences may differ by physician specialty. These results suggest a need for additional research into treatment options for patients with moderate-to-severe CD and UC in Europe.

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P0509 WITHDRAWN

P0510

ASSESSMENT OF VEDOLIZUMAB DISEASE-DRUG-DRUG INTERACTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Disease-drug-drug interactions (DDIs) have been identified in some inflammatory diseases where elevated proinflammatory cytokines can downregulate the expression and/or activity of specific cytochrome P450 (CYP) enzymes, potentially increasing the systemic exposure of drug substrates metabolised by CYPs. Several therapeutic monoclonal antibodies for treating inflammatory conditions that impact cytokines have been reported to normalise CYP expression and thereby reduce exposure to drug substrates. Vedolizumab has a well-established, positive benefit-risk profile in patients with ulcerative colitis (UC) or Crohn's disease (CD) based on extensive clinical trial data and postmarketing experience. Vedolizumab has no known systemic immunosuppressive activity and is not regarded as a direct cytokine modulator.

Aims & Methods: A stepwise assessment was conducted to evaluate the DDI potential for vedolizumab to impact patient exposure to CYP substrate drugs through modulation of pro-inflammatory cytokines. First, a literature review was performed to assess cytokine concentrations and the exposure of commonly used medications metabolised by CYP enzymes in patients with UC or CD versus healthy controls. Next, concentrations of cytokines (IL-6, IL-10, IL-1 β , IL-8, IFN- γ , and TNF- α) and a surrogate biomarker of CYP3A4 activity (ratio of 4 β -hydroxycholesterol to cholesterol) were analysed in stored serum samples (63 UC, 128 CD) from VISIBLE 1 (28 UC) and 2 (59 CD) patients, collected before and during vedolizumab intravenous induction and subcutaneous maintenance treatment of UC and CD, plus 40 commercially obtained healthy control serum samples. Results were descriptively summarised by disease status (UC, CD, or healthy) and by treatment period to explore any potential effect of UC or CD and vedolizumab treatment on CYP activity. Finally, a medical review of the Takeda vedolizumab global safety database was conducted on 5 years of vedolizumab postapproval data to evaluate any evidence of true DDI for reported cases.

Results: The literature review showed that patients with moderately to severely active UC or CD had statistically significantly elevated cytokine concentrations relative to healthy controls; however, these concentrations remained below published levels that could impact CYP expression. Exposure to conventional nonbiologic UC and CD medications (corticosteroids or immunosuppressant drugs) metabolised via CYP3A was comparable between patients and healthy controls. Data from analysed samples showed no trend for higher cytokine concentrations in patients with UC or CD relative to healthy controls except for IFN- γ , which was used to verify the active disease status of patients. Cytokine concentrations were also comparable during baseline, vedolizumab treatment induction, and maintenance phases. Ratios of 4 β -hydroxycholesterol to cholesterol were consistently similar between healthy controls and patients with UC or CD both before and during vedolizumab treatment. A total of 22 adverse event reports of suspected DDIs were identified in the vedolizumab global safety database search. Medical adjudication of these cases did not reveal any relationship to vedolizumab DDIs.

Conclusion: There is a lack of clinically meaningful effect of inflammatory bowel disease on the exposure of CYP substrate drugs resulting from modulation of proinflammatory cytokines. In this study, vedolizumab treatment also did not affect CYP activity, indicating minimal risk of DDIs with vedolizumab treatment of patients with UC and CD.

References: None

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P0511

EFFECTS OF SUBCUTANEOUS VEDOLIZUMAB ON HEALTH-RELATED QUALITY OF LIFE AND WORK PRODUCTIVITY IN PATIENTS WITH CROHN'S DISEASE: RESULTS FROM THE PHASE 3 VISIBLE 2 TRIAL

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Introduction: Patients with Crohn's disease (CD) experience substantial impairment of quality of life (QoL) and productivity. Thus, in addition to clinical efficacy, patient QoL endpoints are critical measures of CD treatment outcome.

Aims & Methods: We evaluated the effects of a subcutaneous (SC) formulation of vedolizumab on clinical remission, QoL, and work productivity based on patient reported outcomes (PROs) in the VISIBLE 2 trial. VISIBLE 2 (NCT02611817; EudraCT 2015-000481-58), was a pivotal, phase 3, randomised, double-blind, placebo-controlled trial evaluating the efficacy and safety of vedolizumab SC as maintenance treatment for moderately to severely active CD. Patients who responded to intravenous (IV) vedolizumab induction by Week 6 were randomised 2:1 to vedolizumab 108 mg SC maintenance (VDZ) or placebo (PBO) every 2 weeks. For this analysis, clini-

cal remission at Week 52 was defined using diary items from the Crohn's Disease Activity Index (CDAI): 2-item PRO2 ≤ 8 (abdominal pain and stool frequency), 3-item PRO3 ≤ 13 (PRO2 items and general well-being), and mean daily stool frequency ≤ 1.5 with abdominal pain ≤ 1 from the last 7 days. Observed mean changes from baseline to Week 52 in the Inflammatory Bowel Disease Questionnaire (IBDQ), the Euro Quality of Life-5D (EQ-5D) scale (3-level), the EQ-5D visual analogue scale (VAS), and the work productivity and activity impairment-CD (WPAI-CD) scores were assessed. **Results:** Induction responders were randomised to and received vedolizumab SC maintenance (N=275) or placebo (N=134) at Week 6. More patients in the VDZ vs PBO arm achieved clinical remission at Week 52 based on PRO2 (40.4% vs 29.1%), PRO3 (40.4% vs 30.6%), and mean daily stool frequency ≤ 1.5 with abdominal pain ≤ 1 (29.1% vs 23.9%). Improvements in QoL and work productivity from baseline were observed at Week 6 following vedolizumab IV induction and sustained through Week 52 in both arms. Mean changes from baseline in IBDQ total scores at Week 52 (VDZ: +63.3 from 107.7; PBO: +55.1 from 109.0) showed QoL improvements, with a trend favouring vedolizumab SC vs placebo. Both arms showed improvements from baseline to Week 52 in mean EQ-5D index score (VDZ: +0.21 from 0.65; PBO: +0.16 from 0.65) and EQ-5D VAS (VDZ: +27.7 from 43.5; PBO: +26.2 from 42.4). Both treatment arms also showed increased work productivity over time, with decreased mean WPAI-CD overall work productivity loss (VDZ: -32.5% from 59.6%; PBO: -28.1% from 58.6%) and activity impairment scores (VDZ: -32.7% from 59.0%; PBO: -28.1% from 59.8%) from baseline to Week 52. Subscores for IBDQ and overall WPAI-CD work productivity loss showed numerically greater improvements for vedolizumab SC vs placebo (Table).

Conclusion: Greater patient QoL and work productivity observed with vedolizumab IV induction and sustained during vedolizumab SC maintenance vs placebo support the clinical benefits of vedolizumab for patients with moderately to severely active CD.

Subscores		Vedolizumab SC (N=275)	Placebo (N=134)		
		Baseline	Changes From Baseline ^a	Baseline	Changes From Baseline ^a
IBDQ ^a	Bowel symptoms	34.8	+20.1	35.1	+17.1
	Emotional function	41.6	+21.9	41.9	+19.5
	Social function	17.5	+11.1	18.0	+9.9
	Systemic symptoms	13.8	+10.2	14.1	+8.6
Overall WPAI-CD work productivity loss, ^b %	Absenteeism ^c	22.7	-13.3	20.4	-13.1
	Presenteeism ^c	53.4	-29.3	53.8	-25.9

IBDQ, Inflammatory Bowel Disease Questionnaire; PBO, placebo; VDZ, vedolizumab; WPAI-CD, work productivity and activity impairment-Crohn's disease.

^aAn increase from baseline indicates an improvement in quality of life.

^bA decrease from baseline indicates less impairment and improved productivity and activity.

^cThe work productivity loss score is a combination of absenteeism and presenteeism.

^dChanges based on 185 patients for IBDQ subscores, 114 patients for absenteeism, and 111 patients for presenteeism.

^eChanges based on 87 patients for IBDQ subscores, 47 patients for absenteeism, and 46 patients for presenteeism.

[Table. Mean changes from baseline to Week 52 in EQ-5D and WPAI-CD work productivity subscores]

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P0512

DISEASE CONTROL AND CHANGES IN INDIVIDUAL TREATMENT OUTCOMES FROM WEEK 14 TO WEEK 52 WITH VEDOLIZUMAB OR ADALIMUMAB IN ULCERATIVE COLITIS: A VARSITY TRIAL POST HOC ANALYSIS

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Introduction: In VARSITY, vedolizumab (VDZ), an anti- $\alpha_4\beta_7$ integrin antibody, achieved superior clinical, endoscopic and histologic outcomes vs adalimumab (ADA), an anti-tumour necrosis factor (TNF) agent, in patients

with moderate-to-severe ulcerative colitis (UC).¹ In recent years, the therapeutic goal for UC has evolved from symptom relief to disease control across multiple outcomes.

Aims & Methods: This VARSITY post hoc analysis evaluated the trajectory of UC key endpoints and disease control with intravenous VDZ vs subcutaneous ADA between early (Week [W]14) and late (W52) time points. Evolution in disease control over time was assessed based on the proportion of patients who maintained, improved, or lost treatment benefit from W14 to W52 for the efficacy endpoints of clinical remission (partial Mayo score of ≤ 2 points and no individual subscore > 1 point), endoscopic improvement (Mayo endoscopic subscore of ≤ 1 point), and histologic improvement (Robarts Histological Index [RHI] score < 5). Data were analysed within treatment arms in the full analysis population and in anti-TNF naïve and anti-TNF experienced subgroups. Observed data without imputation of missing data were reported.

Results: The study included 769 patients with UC (ADA: 386, VDZ: 383). Most patients (56.0% ADA vs 60.8% VDZ) were male, were not using a corticosteroid at baseline (63.7% vs 63.9%) and were anti-TNF naïve (79.0% vs 79.2%). Median UC duration was 4.5 (ADA) and 4.8 (VDZ) years. At W14, clinical remission (40.9% ADA vs 56.4% VDZ), endoscopic improvement (32.6% vs 39.1%), and histologic improvement (28.3% vs 41.7%) were all achieved more frequently with VDZ than with ADA. With both ADA and VDZ, more anti-TNF naïve patients than anti-TNF experienced patients maintained each efficacy outcome from W14 to W52, while the numbers of patients who gained efficacy at W52 was more comparable between anti-TNF naïve and experienced (Table). The additional gain of response in early non-responders was similar between anti-TNF naïve and experienced. In addition, more patients maintained their treatment benefits with VDZ than ADA, in both anti-TNF subgroups, but this was more pronounced in the TNF naïve (eg, 31.1% ADA vs 45.1% VDZ maintained clinical remission). At W52, the overall rate of disease control (composite of clinical remission plus endoscopic and histologic improvement) was higher with VDZ than ADA, especially in the anti-TNF naïve (Table). Further analyses of early predictors for late disease control will be presented.

Conclusion: VDZ treatment maintains greater early disease control than ADA in patients with moderate-to-severe UC from W14 to W52. These observations are more pronounced in patients without prior exposure to anti-TNF agents. These data suggest that VDZ is superior to ADA not only in induction treatment evaluated at W14 but also during the maintenance phase at W52, and that most of the observed treatment differences in anti-TNF naïve patients at W52 were established with early response to treatment that occurred between W0 and W14.

References: 1. Sands BE, et al. *N Engl J Med*. 2019;381(13):1215-1226.

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Gained Outcome	Maintained Outcome	Never Achieved Outcome	Lost Outcome + Missing Status W52	Gained Outcome	Maintained Outcome	Never Achieved Outcome	Lost Outcome + Missing Status W52
ADA Clinical Remission^a (N: 270 / N: 72)^b	VDZ Clinical Remission^a (N: 277 / N: 67)^b						
36 (13.3)/ 9 (12.5)	84 (31.1)/ 10 (13.9)	42 (15.6)/ 14 (19.4)	108 (40.0)/ 39 (54.2)	34 (12.3)/ 7 (10.4)	125 (45.1)/ 20 (29.9)	35 (12.6)/ 16 (23.9)	83 (30.0)/ 24 (35.8)
ADA Endoscopic Improvement^c (N: 265 / N: 72)^b	VDZ Endoscopic Improvement^c (N: 278 / N: 67)^b						
32 (12.1)/ 6 (8.3)	56 (21.1)/ 11 (15.3)	74 (27.9)/ 19 (26.4)	103 (38.9)/ 36 (50.0)	44 (15.8)/ 8 (11.9)	85 (30.6)/ 13 (19.4)	71 (25.5)/ 20 (29.9)	78 (28.1)/ 26 (38.8)
ADA Histologic Improvement^d (N: 261 / N: 71)^b	VDZ Histologic Improvement^d (N: 274 / N: 69)^b						
44 (16.9)/ 10 (14.1)	39 (14.9)/ 4 (5.6)	64 (24.5)/ 23 (32.4)	114 (43.7)/ 34 (47.9)	52 (19.0)/ 9 (13.0)	82 (29.9)/ 16 (23.2)	55 (20.1)/ 18 (26.1)	85 (31.0)/ 26 (37.7)
ADA Disease Control^e at W52 (N: 168 / N: 33)	VDZ Disease Control^e at W52 (N: 203 / N: 41)						
55 (32.7)/ 8 (24.2)	96 (47.3)/ 16 (39.0)						

Note: observed data, no imputation applied. Percentages are based on the number of patients with each endpoint assessed at Week 14.

ADA, adalimumab; TNF, tumour necrosis factor; VDZ, vedolizumab; W, Week.

^aClinical Remission: partial Mayo score of ≤ 2 and no individual subscore > 1 point.

^bNumber of anti-TNF naïve / anti-TNF experienced patients with assessment of the respective endpoint at Week 14.

^cEndoscopic improvement: Mayo endoscopic subscore ≤ 1 .

^dHistologic improvement: Robarts Histological Index score < 5 .

^eDisease control: observed in patients with clinical remission and endoscopic and histologic improvements.

[Table. Changes in Outcomes from W14 to W52 and Disease Control at W52 by Anti-TNF Status (Naïve/Experienced) in ADA (N:305/N:81) and VDZ (N:304/N:79)]

Rheos Medicines, Seres Therapeutics, Shire, Sienna Biopharmaceuticals, Synergy Pharmaceuticals, Takeda, Target PharmaSolutions, Theravance Biopharma, TiGenix, UCB, Valeant Pharmaceuticals North America, Vivelix Pharmaceuticals; Research support: Takeda, Janssen, Theravance Biopharma, Pfizer. EVL: Financial support for research: AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Genentech, Celgene, Receptos, Gilead, Bristol-Myers Squibb, Roberts Clinical Trials; Consultancy: AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Eli Lilly, Celltrion Healthcare, Allergan, Bristol-Myers Squibb, Celgene, Gilead, Genentech, Boehringer Ingelheim. DL: Employee of Takeda; holds Takeda stock or stock options. RAL: Employee of Takeda; holds Takeda stock or stock options. CA: Employee of Takeda; holds Takeda stock or stock options. SS: Consultancy fees: AbbVie, Celltrion, Janssen, Merck, Pfizer, Roche, Takeda.

P0513

VEDOLIZUMAB ACHIEVES CORTICOSTEROID-FREE CLINICAL RESPONSE AND REMISSION IN INFLAMMATORY BOWEL DISEASE: A REAL-WORLD META-ANALYSIS

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Introduction: Vedolizumab (VDZ) is a gut-selective, humanised, anti- $\alpha_4\beta_7$ integrin, monoclonal antibody approved to treat moderately to severely active ulcerative colitis (UC) and Crohn's disease (CD) in adults. Corticosteroids (CS) are frequently used for acute treatment of UC and CD, but should not be used long term because of associated adverse events.^{1,2} VDZ achieved CS-free clinical remission in the GEMINI placebo-controlled randomised studies,^{3,4} yet a thorough understanding of CS-free clinical remission in real-world clinical settings is limited.

Aims & Methods: To evaluate real-world CS-free clinical response and remission in VDZ-treated patients with UC or CD, a systematic literature review of VDZ real-world studies published from January 2014 to October 2018 was conducted using MEDLINE and EMBASE databases, and conference abstracts. Reports with $n < 50$, patients < 18 years old, or off-label VDZ use were excluded. A meta-analysis was performed using the DerSimonian-Laird random-effects model to generate weighted mean rates and corresponding 95% confidence intervals of CS-free clinical response and remission separately for UC and CD at 6 weeks, 10-14 weeks, 6 months, and 12 months.

Results: The meta-analysis included 23 studies (18 UC, 20 CD) reporting CS-free clinical response and remission in VDZ-treated patients (1544 UC, 2748 CD). Weighted mean age was 41.5 (UC) and 40.6 (CD) years, and disease duration before VDZ treatment was 8.0 (UC) and 13.3 (CD) years. Males comprised 54.5% with UC and 41.8% with CD; most patients (70.5% UC, 91.4% CD) had received anti-tumour necrosis factor therapy. Most studies defined CS-free clinical response and remission for UC as complete tapering off CS with clinical response or remission (mostly defined by partial Mayo score) and for CD as absence of oral CS dosing with clinical response or remission (mostly defined by Harvey-Bradshaw Index). For UC, the estimated overall rate of CS-free clinical response was 26.0%, 64.3%, 51.1%, and 58.4% at assessment timepoints of 6 weeks, 10-14 weeks, 6 months, and 12 months, respectively; for CD, rates were 28.4%, 68.2%, 48.4%, and 51.0%. CS-free clinical remission in CD increased after 6 weeks and was 31% at 12 months (Table). This finding was consistent with GEMINI 2 results (30% at 12 months).³ CS-free clinical remission in UC was 47% at 12 months (Table), which was higher than in GEMINI 1 (39% at 12 months).⁴

Conclusion: CS-free clinical response and remission were observed through 12 months of VDZ treatment in patients with UC or CD in real-world clinical practice. This pooled analysis of real-world evidence lends additional support to the clinical benefits of VDZ for long-term maintenance treatment of UC and CD.

Assessment Timepoint	UC		CD	
	Patients, n	Studies, n	Pooled CS-Free CR Rate, % (95% CI)	Pooled CS-Free CR Rate, % (95% CI)
6 weeks	236	2	14.3 (5.6-31.8)	12.9 (7.6, 21.0)
10-14 weeks	1111	13	35.6 (27.9, 44.1)	30.5 (24.3, 37.4)
6 months ^a	992	7	44.5 (30.4, 59.4)	31.4 (21.9-42.7)
12 months ^b	344	4	46.8 (29.3, 65.1)	30.5 (24.4-37.2)

CD, Crohn's disease; CI, confidence interval; CR, clinical remission; CS, corticosteroid; UC, ulcerative colitis.

^a6-month analyses included data reported at 24 to 30 weeks.

^b12-month analyses included data reported at 46 to 54 weeks.

[Table. Pooled Rates of Real-World Corticosteroid-Free Clinical Remission in Vedolizumab-Treated Patients With UC or CD]

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P0514

REAL-WORLD EVIDENCE OF VEDOLIZUMAB ACHIEVING MUCOSAL HEALING AND ENDOSCOPIC IMPROVEMENT IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Vedolizumab (VDZ) is a gut-selective, humanised, monoclonal, $\alpha_4\beta_7$ integrin antibody approved for the treatment of moderately to severely active ulcerative colitis (UC) in adults. Mucosal healing is associated with improved long-term outcomes and considered an important therapeutic goal in UC.¹ GEMINI 1 and VARSITY controlled trials have shown high rates of mucosal healing in VDZ-treated patients with UC.^{2,3}

Aims & Methods: We conducted a systematic literature review on the real-world effectiveness of VDZ in achieving mucosal healing and endoscopic improvement in adult patients with UC. MEDLINE and EMBASE databases, and conference abstracts from January 2014 to October 2018 were searched. Reports with $n < 10$, patient age < 18 years, and off-label VDZ use were excluded. A meta-analysis was performed using the DerSimonian-Laird random-effects model, and weighted mean along with 95% confidence interval were reported for mucosal healing.

Results: A total of 22 reports that examined mucosal healing (18 reports) and endoscopic improvement (5 reports) in VDZ-treated patients diagnosed with UC (N=1,741) were selected for analysis. Mucosal healing at 6 weeks of treatment was analysed despite limited data (2 reports, 83 participants) to enable comparison with GEMINI 1 trial results. Patients had a weighted average age of 41.5 years, were in the majority male (56.4%) and anti-tumour necrosis factor experienced (61.6%), and had a weighted average disease duration before VDZ treatment of 7.6 years. The most common definition for mucosal healing was a Mayo Endoscopic Subscore (MES) ≤ 1 ; other definitions were MES=0, total Mayo score ≤ 1 , or absence of mucosal ulcers and/or erosions. Most studies defined endoscopic improvement as decrease of MES ≥ 1 . The pooled estimate of mucosal healing rate in patients at 6 weeks was 44.8% (N=83) and was similar to GEMINI 1 trial results (40.9%).² This effectiveness was similar in studies with treatment lasting for ≥ 12 months, with a pooled rate of 42.8% (N=494) at 12 months that was comparable to GEMINI 1 (51.6%)² and VARSITY (39.7%)³ trial results (Table). Endoscopic improvement rates assessed at up to 12 months from VDZ initiation ranged from 52.6% to 81.8% in 5 studies.

Conclusion: The pooled estimate of mucosal healing rates in patients with UC in real-world clinical practice were consistent with the results from the GEMINI 1 and VARSITY trials and similar between 6 weeks and 12 months of treatment. High rates of endoscopic improvement were also observed with up to 12 months of VDZ treatment. This study confirms the early benefit of VDZ in achieving mucosal healing among patients with UC in the real-world clinical practice setting.

Timepoint	Patients, n	Studies, n	Mucosal Healing, % (95% CI)
6 weeks	83	2	44.8 (27.1-64.0)
10-14 weeks	521	11	46.3 (36.9-56.1)
6 months ^a	790	7	38.0 (26.4-51.3)
12 months ^b	494	5	42.8 (29.6-57.0)

CI, confidence interval.

^a6 months analysis includes data reported at 24-30 weeks.

^b12 months analysis includes data reported at 46-54 weeks.

[Table. Real-World Evidence of Pooled Estimates of Overall Mucosal Healing Rates in Vedolizumab-Treated Patients With Ulcerative Colitis]

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P0515

FECAL CALPROTECTIN AS A SURROGATE MARKER OF CLINICAL REMISSION, CLINICAL RESPONSE, ENDOSCOPIC IMPROVEMENT, AND HISTO-ENDOSCOPIC MUCOSAL HEALING: UNIFI INDUCTION STUDY

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Introduction: Previously we reported the safety and efficacy of ustekinumab (UST) therapy for the treatment of moderately to severely active UC patients in the Phase 3 UNIFI studies.¹ The objective of these analyses was to assess, using data from the UNIFI induction study,¹ the operating properties of fecal calprotectin (FCP) with clinical remission, clinical response, endoscopic improvement, and histo-endoscopic mucosal healing (HEMH) as endpoints.

Aims & Methods: The UNIFI induction study was a multicenter, randomized, placebo- (PBO) controlled trial that randomized patients to intravenous dosing with PBO, UST 130 mg and UST ~6 mg/kg.¹ FCP was measured at Weeks (W) 0 (baseline), 2, 4 and 8 using the CALPRO® Calprotectin ELISA Test. The area under the Receiver Operating Characteristic curve (AUC-ROC) was used to assess the accuracy of absolute change and percent (%) change from baseline in FCP at W4 for prediction of clinical response, clinical remission, endoscopic improvement, and HEMH at W8 for UST 6 mg/kg-treated patients, (the FDA approved induction dosage). Sensitivity, specificity, and negative and positive likelihood ratios of cut-off % change in FCP from baseline at W4 were also estimated for the W8 outcomes.

Results: AUC-ROC analyses demonstrated % change from baseline in FCP at W4 predicted efficacy outcomes at W8 more accurately than the corresponding absolute change from baseline at W4: HEMH (0.70 vs 0.58), clinical remission (0.65 vs 0.54), endoscopic improvement (0.64 vs 0.58), and clinical response (0.60 vs 0.58), respectively. The % change from baseline in FCP at W4 had the best accuracy in predicting W8 HEMH compared with its diagnostic accuracy in predicting clinical remission, endoscopic improvement, and clinical response at W8. Sensitivity, specificity, and negative and positive likelihood ratios for 50% and 80% change from baseline in FCP at W4 in predicting efficacy outcomes at W8 are shown in (Table 1).

Endpoint at W8	Cutoff for % Reduction from Baseline FCP at W4 ^{a,b}	% Pts achieving the endpoints (<% cutoff vs $\geq$ % cutoff)	Sensitivity	Specificity	Likelihood Ratio Negative ^c	Likelihood Ratio Positive ^c
HEMH ^{d,e,f,g}	50	9.6% (15/157), 25.0% (34/136)	0.69	0.58	0.53	1.66
	80	10.5% (24/228), 38.5% (25/65)	0.51	0.84	0.59	3.11
Clinical Remission ^{d,e,h}	50	10.1% (16/159), 19.9% (28/141)	0.64	0.56	0.65	1.44
	80	10.3% (24/232), 29.4% (20/68)	0.45	0.81	0.67	2.42
Endoscopic Improvement ^{d,e,i}	50	18.2% (29/159), 34.0% (48/141)	0.62	0.58	0.65	1.49
	80	19.8% (46/232), 45.6% (31/68)	0.40	0.83	0.72	2.43
Clinical Response ^{d,e,i}	50	54.7% (87/159), 69.5% (98/141)	0.53	0.63	0.75	1.42
	80	58.6% (136/232), 72.1% (49/68)	0.26	0.83	0.88	1.60

^aWeight-range based UST doses approximating 6 mg/kg: 260 mg (weight ≤ 55 kg), 390 mg (weight > 55 kg and ≤ 85 kg), 520 mg (weight > 85 kg). ^bPatients (pts) who had a prohibited change in concomitant UC medication or an ostomy or colectomy prior to W4 had their baseline FCP value forward to that timepoint.

^cPts who had missing data for FCP at W4 had their last available value carried forward to that timepoint.

^dNegative likelihood ratio: (1-sensitivity)/specificity; Positive likelihood ratio: sensitivity/(1-specificity). ^ePts who had a prohibited change in concomitant UC medication or an ostomy or colectomy prior to the W8 visit were considered not to be in clinical response, clinical remission, endoscopic improvement, or HEMH at W8. ^fPts who were missing all of the Mayo components at W8 visit were considered not to be in clinical response or clinical remission at W8; pts who had a missing endoscopy score were considered not to have endoscopic improvement at W8. Pts who had a missing endoscopy score or were missing any of the components pertaining to histologic improvement endpoint (i.e., assessment of neutrophils in epithelium, crypt destruction, or erosions or ulcerations or granululations) at W8 were considered not to have HEMH. ^gHEMH: both histologic improvement (absence of erosion or ulceration, absence of crypt destruction, and $< 5\%$ of crypts with epithelial neutrophil infiltration) and endoscopic improvement (endoscopy score of 0 or 1). ^hPts whose HEMH status could not be determined at W8 due to an unevaluable biopsy (i.e., a biopsy that was collected, but could not be assessed due to sample preparation or technical errors) were excluded. ⁱClinical remission: Mayo score ≤ 2 points, with no individual subscore > 1 . Endoscopic improvement: Endoscopy score of 0 or 1. ^jClinical response: decrease from baseline in the Mayo score by $\geq 30\%$ and ≥ 3 points, with either a decrease from baseline in the rectal bleeding subscore ≥ 1 or a rectal bleeding subscore of 0 or 1.

[Sensitivity, specificity, likelihood ratios:50%/80% reduction from baseline FCP at W4 in predicting W8 efficacy outcomes;pts randomized to UST6mg/kg*]

Conclusion: Overall, these data suggest that early improvements in FCP may be used as a surrogate marker of clinical outcomes after intravenous induction of UST in UC patients.

References: 1. Sands BE, et al. *N Engl J Med*. Sept 26, 2019; 381(13):1201-1214.

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P0516

EFFICACY OF USTEKINUMAB AT THE END OF MAINTENANCE IN ULCERATIVE COLITIS PATIENTS RECEIVING 6 MG/ KG INDUCTION POSOLOGY. DATA FROM UNIFI TRIAL

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Introduction: The efficacy of ustekinumab in ulcerative colitis was assessed in UNIFI clinical program (1). Data already reported at the end of maintenance (UNIFI week 44) include patients receiving 2 different induction dosing regimens: a single 130 mg ustekinumab vial and a tiered ustekinumab 6 mg/kg dose. However, the approved posology described in EMA Summary of Product Characteristics (SmPC) (2) is an induction regimen of 6 mg/kg followed by a maintenance regimen with ustekinumab 90 mg each 12 weeks or each 8 weeks. Although clinical efficacy at the end of UNIFI maintenance (week 44) in patients that responded to the approved 6 mg/kg induction regimen have been partially reported (3,4), clinical remission and mucosal healing by previous biologic treatment and by ustekinumab maintenance posology subgroups have not been reported.

Aims & Methods: To report clinical remission and mucosal healing at the end of UNIFI maintenance (week 44) in patients that responded to the approved ustekinumab 6 mg/kg induction regimen and completed maintenance treatment, analyzing separately the subgroups of patients with or without previous biologic failure and receiving maintenance regimen with ustekinumab 90 mg each 12 weeks or each 8 weeks.

Results: Efficacy outcomes at the end of UNIFI maintenance (week 44) are presented in Table 1, including results as reported in the original publication (1) (considering patients that responded to both induction regimens), and results considering only patients responding to 6 mg/kg induction regimen, both for the overall population (3) and for the different subgroups (previous failure to biologic treatment and received ustekinumab maintenance posology) for clinical response (4), clinical remission and mucosal healing.

Table 1: (a) Responders to ustekinumab 130 mg or 6 mg/kg eight weeks after induction; (b) in patients with clinical response after induction with ustekinumab; (c) Responders to ustekinumab 6 mg/kg eight weeks after induction; (I) Induction; (M) Maintenance. The term "Mucosal Healing" is considered as "Endoscopic Improvement" in some references (1).

Conclusion: As reported for clinical response (4), clinical remission and mucosal healing at the end of maintenance in patients with clinical response to ustekinumab 6 mg/kg approved induction regimen are higher compared to UNIFI reported data combining the two induction regimens in the trial, both for patients with and without previous biologic failure and for both ustekinumab maintenance regimens. These results are expected to be more representative of the real-life clinical efficacy of ustekinumab, as all patients received the 6 mg/kg approved induction regimen.

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	Placebo (M) N=175 (a)	90 mg UST every 8 weeks (M) N=176 (a)	90 mg UST every 12 weeks (M) N=172 (a)	6 mg/kg (I)- 90 mg UST every 8 weeks (M) N=70 (c)	6 mg/kg (I)- 90 mg UST every 12 weeks (M) N=69 (c)
Clinical Remission at week 44 (b)	24%	44%	38%	48,6%	49,3%
Clinical remission in patients who failed conventional therapy, but not a biologic	31% (27/87)	48% (41/85)	49% (50/102)	51,6% (16/31)	55,6% (25/45)
Clinical remission In patients who failed biological therapy	17% (15/88)	40% (36/91)	23% (16/70)	46,2% (18/39)	37,5% (9/24)
Maintenance of clinical response through week 44 (b)	45%	71%	68%	72,9%	82,6%
Clinical response In patients who failed conventional therapy, but not a biologic	51% (44/87)	78% (66/85)	77% (78/102)	74,2% (23/31)	88,9% (40/45)
Clinical response In patients who failed biological therapy	39% (34/88)	65% (59/91)	56% (39/70)	71,8% (28/39)	70,8% (17/24)
Mucosal Healing (b)	29%	51%	44%	54,3%	56,5%

[Table 1]

P0517

TREATMENT OF ADULTS WITH THE CLOSTRIDIA STRAIN LIVE BIOTHERAPEUTIC PRODUCT VE202 RESULTS IN SUSTAINED AND DURABLE COLONIZATION OF THE HEALTHY HUMAN GUT

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Introduction: IBD is characterized by bacterial dysbiosis and mucosal immune dysregulation. VE202 is a live biotherapeutic drug product (LBP) being developed for the treatment of IBD. It is comprised of commensal, nonpathogenic *Clostridia* strains derived from a healthy donor that have been shown to induce regulatory T cells in preclinical models¹. 11 and 16 strain consortia VE202 LBPs are under evaluation. We assessed the safety, tolerability, and pharmacokinetics of colonization (presence and abundance) of VE202 strains following dosing of the 11 strain LBP in healthy adult volunteers (HV) throughout the 6-month duration of a FIH study.

Aims & Methods: HVs were enrolled in a phase I double-blind, placebo-controlled study (NCT03723746; n=74 total subjects; 6 cohorts). Single day (cohorts 1 and 2) and multi-day (cohorts 3-6; 14 days) oral dosing of a low or high CFU dose of VE202, or placebo, was administered. Two multi-day dosing cohorts (4 and 6) were pretreated with vancomycin (125mg, qid) for

P0518

RESPONSE TO INDUCTION TREATMENT WITH BIOLOGICALS
IN A MULTICENTER, PROSPECTIVE COHORT OF BIOLOGICAL-NAÏVE
IBD PATIENTS - PRELIMINARY RESULTS FROM THE DANISH IBD
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Introduction: The use of biologicals is a paradigm shift in the manage-
ment of inflammatory bowel disease (IBD). Despite increasing use and an
expanding panel of biological agents, previous studies have reported high
rates of primary non-response (PNR).**Aims & Methods:** We aimed to assess response to induction therapy with
biological agents in a real-world prospective cohort of biological-naïve
IBD patients.The Danish IBD Biobank Project (www.ibdbiobank.com) is a multicenter,
prospective cohort including adult, bio-naïve IBD patients who initiated
biological therapy from May 1 st, 2019 and onward at four study centers
covering three of five health regions in Denmark. Data on disease char-
acteristics, medication use, surgery, and response to biological treatment
were collected prospectively. Data from three centers were included in
this study. Response to induction therapy was assessed in patients who
had completed at least three treatments with a first-line biological drug.
Response was defined as a decrease in Simple Clinical Colitis Activity In-
dex (SCCAI) more than one from baseline in ulcerative colitis (UC) and a
decrease in Harvey Bradshaw Index (HBI) more than 3 in Crohn's disease
(CD). Remission was defined as SCCAI < 3 in UC and HBI < 5 in CD. PNR
was defined as lack of clinical response or need of surgery within the in-
duction period. Baseline characteristics between PNR and non-PNR were
compared using Chi-square test.**Results:** As of April 20th, 2020, a total of 212 bio-naïve IBD patients (52%
UC, 45% CD, 3% IBDU) at a mean age of 41 years were included. In UC,
31% presented with extensive colitis, and in CD, 23% presented with com-
plicated behaviour and 13% had perianal fistula at diagnosis. Biological
treatment was initiated at a median of 3 years (IQR 0-9) in UC and 1.5 years
(IQR 0-8.5) in CD after diagnosis. Overall, treatment was initiated within
two years in 49%. In 13% UC and 18% CD patients, the biological drug was
used concomitantly with an immunomodulator (IM).In UC, 72% initiated treatment due to chronic active UC and 26% due to
acute severe UC. In CD, 72% and 14% initiated treatment due to luminal
and fistulizing CD. Infliximab was the most frequent first-line drug (96%
UC, 94% CD, all IBDU) in accordance with the Danish national treatment
guidelines. Adalimumab was used as first-line drug in 2% UC and 3% CD
patients, four patients received vedolizumab as first-line.Among 165 (51% UC, 46% CD, 3% IBDU) who completed induction ther-
apy, 11% UC and 8% CD underwent major surgery and 10% (10 UC, 5
CD) switched to a second biological drug. Response and remission were
evaluated in 107 patients. At baseline, 7% UC and 38% CD were in clini-
cal remission, but initiated biological due to endoscopic or biochemical
activity (59%), perianal CD (14%), IM intolerance (14%) or as prevention
against postoperative recurrence (9%). Response was achieved in 64% UCfive days prior followed by a one-day washout prior to dosing. Each sub-
ject provided 15-39 stool samples during the study (2,247 samples total).
Bacterial DNA was extracted from stool for VE202 strain quantification via
qPCR with strain specific primers. PK was measured as the number of de-
tected strains, relative abundance (RA), and strain colonization duration.**Results:** Colonization kinetics (CK) of a single day of dosing without
vancomycin pretreatment did not result in increased detection of VE202
strains. In multiple day dosing cohorts, vancomycin pretreatment reduced
gut microbial density and was required for sustained detection of VE202
compared to non-vancomycin pre-treated cohorts. In cohorts 4 and 6,
VE202 rapidly increased in detection within 2 days of dosing and peaked at
day 7 and day 8 (Tmax) with a mean RA of 18.84% and 24.32% respectively
(Table 1). In these cohorts, VE202 strains were detected up to 6 months
post-treatment with mean 7.6 and 8.9 total strains and RA 0.83% and
1.00%, respectively. VE202 strains were also detected in vancomycin pre-
treated placebo cohorts (2.2 and 3.2 mean total strains and RA of 0.25%
and 1.56%, respectively, 6 months post-treatment).**Conclusion:** VE202 strains rapidly, abundantly, and durably colonize the
gut of healthy volunteers above natural background strains detected by
qPCR. Dense longitudinal sampling and inclusion of placebo controls em-
ployed in this study demonstrate that patterns of colonization dynamics
correlate with dose and are influenced by antibiotic pre-treatment. Un-
expectedly, placebo antibiotic pre-treated subjects co-housed with active
drug treated subjects also demonstrated low level VE202 strain specific
colonization although at significantly lower RA levels. Metagenomic profil-
ing currently in progress will assess VE202's impact on global microbiome
community structure.

Antibiotic	Vanco- mycin	No Van- comycin							
Treatment	VE202	Placebo	VE202	Placebo					
Dose	Low n=10	High n=10	Low n=4	High n=4	Low n=10	High n=10	Low n=4	High n=4	
Time									
Pre-Van- comycin	0.0 +/- 0.0	0.1 +/- 0.1	0.0 +/- 0.1	0.0 +/- 0.0	NA	NA	NA	NA	
Pre-Dose	0.0 +/- 0.0	0.0 +/- 0.0	0.0 +/- 0.1	0.0 +/- 0.0	0.0 +/- 0.1	0.0 +/- 0.0	0.0 +/- 0.0	0.0 +/- 0.0	
24h Post First Dose	0.2 +/- 0.6	0.9 +/- 2.7	0.0 +/- 0.0	0.0 +/- 0.0	0.0 +/- 0.1	0.3 +/- 0.2	0.0 +/- 0.0	0.0 +/- 0.0	
Day 3	2.4 +/- 6.1	7.8 +/- 13.5	0.0 +/- 0.1	0.0 +/- 0.0	0.0 +/- 0.0	0.2 +/- 0.3	0.0 +/- 0.1	0.0 +/- 0.0	
Day 7	18.8 +/- 29.4	21.0 +/- 20.1	0.9 +/- 1.4	0.1 +/- 0.2	0.0 +/- 0.0	0.7 +/- 1.2	0.0 +/- 0.1	0.0 +/- 0.0	
Day 8	14.6 +/- 23.2	24.3 +/- 22.1	1.9 +/- 2.6	0.4 +/- 0.7	0.0 +/- 0.0	0.2 +/- 0.2	0.0 +/- 0.1	0.0 +/- 0.0	
Final Day Dose (Day 14)	7.9 +/- 13.7	23.9 +/- 27.2	3.5 +/- 4.5	1.5 +/- 2.0	0.0 +/- 0.1	3.0 +/- 8.0	0.1 +/- 0.1	0.0 +/- 0.0	
FU WEEK 3	5.5 +/- 5.8	14.4 +/- 15.0	2.4 +/- 2.3	3.7 +/- 4.4	0.1 +/- 0.1	0.4 +/- 1.1	0.0 +/- 0.0	0.0 +/- 0.0	
3M End of Study	2.3 +/- 2.6	1.8 +/- 1.4	0.4 +/- 0.3	1.5 +/- 2.3	0.2 +/- 0.5	0.1 +/- 0.1	0.0 +/- 0.0	0.0 +/- 0.1	
6M Follow-up	0.8 +/- 0.5	1.0 +/- 1.3	0.3 +/- 0.2	1.6 +/- 1.8	0.2 +/- 0.6	0.0 +/- 0.0	0.0 +/- 0.0	0.0 +/- 0.0	

[Mean Relative abundances (%) of total VE202 strains in the stool of
multiple day dosed subjects at collection timepoints during the Phase 1 HV
study.]**Disclosure:** Authors are Employees and Shareholders of Janssen R&D
(Johnson and Johnson)

and 43% CD ($p=0.06$), clinical remission was achieved in 30% UC and 40% CD patients. Extensive disease in UC significantly increased the risk of PNR ($p=0.03$), but time to biological use, age, IM and corticosteroid use within two months before initiation of biological drug did not.

Conclusion: In this prospective, multicenter cohort of bio-naïve IBD patients, PNR rate was high and was significantly increased in patients with extensive UC. Although biologicals were started within two years from diagnosis in half of all patients, clinical remission was achieved in only one third. This indicates a need to identify response indicators in order to target biological treatment to the individual patient.

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P0519

COMPARATIVE BIOAVAILABILITY OF NOVEL CYCLOSPORINE FORMULATIONS VERSUS REFERENCE ORAL CYCLOSPORINE IN HEALTHY SUBJECTS UNDER FASTING CONDITIONS

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Introduction: A novel formulation of cyclosporine (CyCol) was designed to deliver active drug directly to the colon, thus allowing for precise targeting of inflamed mucosal epithelium typical for ulcerative colitis (UC) while limiting systemic toxicity.

Aims & Methods: This study aimed to compare the amount of unchanged drug excreted in faeces and the rate and extent of absorption of CyCol fast release, intermediate release, and delayed colon release as compared to oral cyclosporine immediate release (reference comparator) under fasting conditions.

A total of 18 healthy subjects (12 females; 6 males) participated in this single-centre, randomised, single-dose, open-label, 4-period, 4-sequence cross over phase-1 study performed under fasting conditions. Subjects were confined at least 10 hours prior to drug administration until approximately 28 hours post-dose on the morning of Day 2 (or until they had defecated). Faeces were collected from 12 to 28 hours after dosing. CyCol fast, intermediate, and delayed colon release cyclosporine, and oral cyclosporine immediate release were administered in each study period as a single dose of 75 mg (3 x 25 mg capsules). Treatment phases were separated by washout periods of 7 days. Data from all subjects completing at least one period, and for whom the pharmacokinetic (PK) profile could be adequately characterised, were used for PK and statistical analyses.

Results: CyCol fast release was anticipated to be released in the small intestine where it is expected to be systemically absorbed, CyCol intermediate release was expected to initiate its release in the ileum and throughout the colon, and CyCol delayed colon release was expected to initiate its release in the ascending colon and throughout the colon. A summary of PK parameters for each timed-release formulation is given in Table 1. A statistically significant difference was detected between treatments for T_{max} using Friedman's test. Median T_{max} for CyCol intermediate release and delayed colon release were longer (5.00 h) when compared to CyCol fast release (2.00 h) and the reference drug (1.25 h). CyCol fast release, which is the closest to the comparator PK profile, had a lower rate and extent of

absorption when compared to the reference and CyCol intermediate and delayed colon release had significantly lower rates and extent of absorption when compared to the reference. A total of 26 treatment-emergent adverse events (TEAEs) were reported, most were mild or moderate, none, severe. A similar proportion of subjects reported TEAEs among all four treatments. CyCol levels in the faeces were higher in all groups compared to the reference.

Conclusion: All formulations were safe and well tolerated, with no major side effects and similar safety profiles, particularly with respect to the number of subjects reporting TEAEs. The results show that the delayed colon release CyCol formulations are associated with less absorption and lower systemic exposure of drug when compared to the reference.

Mean $\pm$ SD (CV%)	Whole Blood Concentration			
	CyCol	Reference Comparator (Oral Cyclosporine Immediate Release)		
	Fast Release	Intermediate Release	Delayed Colon Release	
Number of subjects	17	17	18	17
AUC ₀₋₄ (ng x h/mL)	1212.52 $\pm$ 297.62 (24.55)	609.89 $\pm$ 280.15 (45.93)	408.49 $\pm$ 231.01 (56.55)	1582.20 $\pm$ 358.09 (22.63)
AUC _{0-inf} (ng x h/mL)	1257.83 $\pm$ 312.14 (24.82)	672.07 $\pm$ 296.71 (44.15)	474.37 $\pm$ 247.93 (52.27)	1639.78 $\pm$ 371.52 (22.66)
C _{max} (ng/mL)	321.33 $\pm$ 87.61 (27.27)	138.28 $\pm$ 63.54 (45.95)	82.81 $\pm$ 48.01 (57.98)	594.66 $\pm$ 117.01 (19.68)
Residual Area (%)	3.55 $\pm$ 0.71 (20.12)	10.72 $\pm$ 8.10 (75.50)	15.38 $\pm$ 12.69 (82.52)	3.52 $\pm$ 0.77 (21.87)
T _{max} (h)	2.00 (1.25-3.00)	5.00 (5.00-8.00)	5.00 (5.00-10.0)	1.25 (1.00-1.75)
K _{el} (1/h)	0.1105 $\pm$ 0.0113 (10.25)	0.0863 $\pm$ 0.0259 (30.01)	0.0822 $\pm$ 0.0232 (28.20)	0.1037 $\pm$ 0.0103 (9.97)
T _{1/2 el} (h)	6.33 $\pm$ 0.61 (9.70)	8.72 $\pm$ 2.76 (31.66)	9.49 $\pm$ 4.55 (47.96)	6.75 $\pm$ 0.77 (11.43)

*Median (Min-Max).

AUC₀₋₄, area under the concentration-time curve from time zero to time of last non-zero concentration; AUC_{0-inf}, area under the concentration-time curve from time zero to infinity (extrapolated); C_{max}, maximum observed concentration; CV, coefficient of variation; K_{el}, elimination rate constant; SD, standard deviation; T_{1/2 el}, elimination half-life (equivalent to t_{1/2}); T_{max}, time of observed C_{max}.

[Table 1: Summary of pharmacokinetic parameters by treatment arm]

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P0520

MESALAZINE INDUCES EARLY HISTO-ENDOSCOPIC MUCOSAL HEALING IN ACTIVE MILD-MODERATE ULCERATIVE COLITIS: POST-HOC ANALYSIS OF POOLED DATA FROM 4 DOUBLE-BLIND, DOUBLE-DUMMY, MULTICENTER, RANDOMIZED TRIALS

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Introduction: Endoscopic mucosal healing has been defined as valuable endpoint of induction therapy in active ulcerative colitis (UC). Recently, also histological remission has emerged for superior long-term clinical outcomes. Combined histo-endoscopic mucosal healing may be a new useful treatment target for patients with active ulcerative colitis.

Aims & Methods: To determine the rate of histo-endoscopic mucosal healing in patients with active ulcerative colitis of mild or moderate activity treated with granulated mesalazine for 8 weeks.

Active UC patients participating in the SAG-2 (1), SAG-15 (2), SAG-26 (3) or BUC-57 (4) studies, having an Endoscopic Index (EI) >3 and a clinical mild (Clinical Activity Index [CAI] >4 and ≤8) or moderate (CAI >8) baseline disease activity were eligible for this post-hoc analysis. Patients were treated with 1.5g/d, 3g/d or 4.5g/d mesalazine granules for 8 weeks. Assessments used were CAI and EI acc. to Rachmilewitz and Histology Index (HI) acc. to Riley. Combined histo-endoscopic mucosal healing was defined as EI ≤1 and HI ≤1 at week 8 (last observation carried forward [LOCF]).

Results: A total of 860 patients were included into the analysis. At baseline, 568 patients had an UC of mild and 292 of moderate disease activity. Histo-endoscopic mucosal healing was achieved by 25.3% of the patients at week 8 (LOCF) in the total population (see table 1A). High dosage of 3g/d mesalazine led to significant higher rates of histo-endoscopic mucosal healing compared to 1.5g/d ($p=0.0257$ [2-sided]), i.e. 17.9% with 1.5g/d, 27.0% with 3g/d and 25.6% under 4.5g/d mesalazine. The differ-

ence between low dose (1.5g/d) and higher doses of mesalazine (3g/d or 4.5g/d) was even more pronounced when only moderate UC patients were considered: 11.9% with 1.5g/d, 24.9% with 3g/d and 24.3% under 4.5g/d mesalazine. Results of the 4.5g/d mesalazine group were comparable to the results of 3g/d mesalazine group. Proportion of patients with histo-endoscopic mucosal healing was higher ($p=0.28$ [2-sided]) in patients with mild activity (26.6%) compared to patients with moderate activity (22.9%). Results of histo-endoscopic mucosal healing are reflected by the endoscopic and histologic remission rates (see table 1B).

Mesalazine Dose Group	1.5g/d	3g/d	4.5g/d	Total
A: Rates of histo-endoscopic mucosal healing				
	%	n/N	%	n/N
Total	17.9%	26/145	27.0%	169/625*
Mild Activity	20.4%	21/103	28.2%	116/412
Moderate Activity	11.9%	5/37	24.9%	53/213
B: Histologic and endoscopic remission rates				
	%	n/N	%	n/N
EI ≤1	22.1%	32/145	33.6%	210/625
HI ≤1	46.2%	67/145	53.6%	335/625

[Table 1]

* $p=0.0257$ (2-sided) for comparison of 3g/d mesalazine group vs. 1.5g/d group.

Conclusion: Short-term treatment with granulated mesalazine induced rapid histo-endoscopic mucosal healing in a significant proportion of mildly or moderately active UC patients. Higher doses of mesalazine were superior to the low dose of 1.5g/d. A mesalazine dose of 3g/d was found as the optimal dose, confirming previous results on other endpoints (1).

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P0521

VEDOLIZUMAB IV VERSUS ADALIMUMAB TO TREAT MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS: COST-EFFECTIVENESS FROM A US PRIVATE PAYER PERSPECTIVE

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Introduction: VARSITY (NCT02497469) is the first head-to-head trial comparing 2 biologic therapies, intravenous vedolizumab (VDZ IV) and subcutaneous adalimumab (ADA), in adult patients with moderately-to-severely active ulcerative colitis (UC).¹ We evaluated the cost-effectiveness of VDZ IV vs ADA from a US payer perspective using efficacy data from the VARSITY clinical trial.

Aims & Methods: We applied a cohort decision tree model with a time horizon of 52 weeks. Simulated cohorts included patients with or without prior TNF inhibitor (TNFi) therapy. Induction consisted of VDZ IV (300 mg in Weeks 0, 2, and 6) or ADA (Day 1: 160 mg; Day 15: 80 mg) for a 6-week period. Responders proceeded to maintenance treatment with VDZ IV (300 mg every 8 weeks) or ADA (40 mg every 2 weeks). Remission was defined as a full Mayo score of ≤2, with no subscore >1, and remit-

ters persisted in that state for the remainder of the model. Patients with inadequate response to induction or a serious adverse drug reaction (ADR) switched to other biologics. Patients who were intolerant to biologics received corticosteroids with or without curative surgery. Clinical data (probabilities of response, remission, and ADRs) were derived from the VARSITY clinical trial. Direct medical costs (2019 US\$) were drawn from the literature and included drug acquisition and administration, routine monitoring, toxicity management, and ADRs. Utilities were also drawn from the literature. Accumulated direct medical costs and quality-adjusted life years (QALYs) were evaluated and used to determine the incremental cost-utility ratio. Univariate and scenario sensitivity analyses were conducted.

Results: Over a 52-week modeled horizon, the VDZ IV cohort was more likely to achieve clinical remission (23% vs 15%), and accumulated lower direct medical costs (\$66,749 vs \$73,015) and more QALYs (0.71 vs 0.61) compared with ADA. Outcomes were most sensitive to the probability of experiencing an ADR during induction and the relative proportions of TNFi-naïve and TNFi-experienced patients.

Conclusion: The clinical foundation of this model is predicated primarily on head-to-head evidence from the phase 3 VARSITY trial. Combined with costs and utilities from the literature, these outcomes demonstrate that VDZ IV was the dominating treatment strategy (ie, more effective and less costly) vs ADA for the treatment of moderately-to-severely active UC from a private payer perspective in the US.

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P0522

CLINICAL EFFICACY, DRUG SUSTAINABILITY AND RESULTS FROM THERAPEUTIC DRUG MONITORING IN CROHN'S DISEASE PATIENTS TREATED WITH USTEKINUMAB - 1-YEAR FOLLOW-UP OF A PROSPECTIVE, NATIONWIDE, MULTICENTER COHORT FROM HUNGARY

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Introduction: Ustekinumab (UST) is one of the more recent biological agents used in the treatment of inflammatory bowel diseases (IBD), and inhibits the inflammatory cascade by binding to the human cytokines interleukin (IL)-12 and IL-23. Although efficacy and safety of UST have been

demonstrated through randomized trials, data from “real-life” prospective cohorts are still of great interest. UST has been introduced into public health reimbursement in Hungary in 2019.

Aims & Methods: Our aim was to evaluate the clinical efficacy, drug sustainability, frequency of dose intensification, results from therapeutic drug monitoring, and other predictive factors in UST treated Crohn's disease (CD) patients using a prospective, nationwide, multicenter cohort from Hungary. Patients were consecutively enrolled in this cohort between 2019 January and 2020 January from 5 academic centers and 5 county hospitals. Data from patient demographics, disease phenotype, treatment history (surgical history, prior and present medical therapies), clinical disease activity, biochemical markers (C-reactive protein - CRP), and therapeutic drug monitoring were captured. Clinical remission/response was defined using the Crohn's Disease Activity Index (CDAI), Harvey Bradshaw Index (HBI), and fistula drainage assessment. Evaluations were performed at week8 (post-induction), w16-20, w32-36, and w54-56 follow-up visits.

Results: In our preliminary analysis n=114 CD patients were included with a median follow-up time of 42 weeks (IQR: 22-59w) [61.4% female; age 37.2±13.2 years; disease duration of median 11y, IQR: 7-17y]. Based on the Montreal classification, disease behavior was B1:60.4% / B2:18.9% / B3:20.7%, whereas disease location was L1:20.8% / L2:29.2% / L3:47.9% / L4(+L1-3):2%. Perianal manifestation was present in 42.5% of the patients. Previous anti-TNF exposition was 98.2% (both infliximab and adalimumab: 61.6%), while previous vedolizumab failure was 28.6% among the study population. Clinical response and remission rates among patients with moderate-to-severe clinical activity at baseline were 83.8% and 54.1% using CDAI, and 85.7% and 36.5% based on HBI scores after induction treatment (w8). Composite clinical (CDAI< 150) and biomarker (CRP< 10mg/L) remission rates were 29.9%; 29.4% and 29.5% at w8/w16-20/w32-36. Steroid free remission rates were 33.3%; 59.0% and 42.2% based on CDAI at w8/w16-20/w32-36. Drug sustainability was high with 91.7% (SD: 2.8) of patients remaining on treatment at week 32. Probability of dose intensification was high and introduced early in the treatment, 46.8% (SD: 5.0) at week 32. Patients with complex disease phenotype (B2/B3) had higher probability for dose intensification compared to luminal disease phenotype (log-rank: p=0.01).

Conclusion: Ustekinumab displayed good drug sustainability and clinical efficacy in a population with severe disease phenotype and high rates of previous anti-TNF failure, however frequent and early dose intensification was required. Final data on the 1-year follow-up and results from therapeutic drug monitoring will be presented at the conference upon acceptance.

Disclosure: Nothing to disclose

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Introduction: Despite their implementation as inclusion and endpoint criteria in clinical trials of Crohn's disease (CD), the prognostic value of patient-reported outcomes (PROs) remains unclear. This analysis aims to evaluate the association between severity of baseline CD PROs, abdominal pain (AP) and stool frequency (SF), and the ability to achieve clinical and endoscopic outcomes.

Aims & Methods: This *post-hoc* analysis of the SONIC study (NCT0094458; YODA #2020-4234) included 421 patients to evaluate the relationship of baseline PRO variables, AP and SF with week 26 clinical remission (CDAI < 150), PRO2 remission (mean score AP ≤ 1 and SF ≤ 1.5, or AP ≤ 1 and SF ≤ 3), and corticosteroid-free clinical remission. For the outcome of endoscopic remission (absence of mucosal ulceration), data from 158 subjects who had baseline and week 26 endoscopic assessments were included. The relationship between baseline PROs and the outcomes of interest at week 26 were evaluated using multivariate logistic regression models adjusted for confounders.

Results: No significant differences were found when comparing patients with higher baseline PRO scores to lower scores in the odds of achieving clinical remission at week 26 [severe vs. not severe AP: OR 1.07, 95% CI 0.62-1.85, p=0.819; mod-severe vs. not severe SF: OR 0.91 (0.60-1.39), p=0.673]. Similarly, no significant differences were found between patients with higher baseline PRO scores to patients with lower scores in the odds of achieving corticosteroid-free clinical remission at week 26 [severe vs. not severe AP: OR 1.08, 95% CI 0.62-1.87, p=0.783; mod-severe vs. not severe SF: OR 0.90, 95% CI 0.59-1.37, p=0.614]. Patients with moderate to severely elevated SF at baseline were less likely to achieve PRO2 remission, regardless of the PRO2 remission definition used [mean score AP ≤ 1 and SF ≤ 1.5: OR 0.44, 95% CI 0.29-0.66, p<0.0001; mean score AP ≤ 1 and SF ≤ 3: OR 0.63, 95% CI 0.41-0.97, p=0.035]. No significant differences were observed when comparing patients with higher baseline PRO scores to lower scores in the likelihood of achieving endoscopic remission [severe vs. not severe AP: OR 0.78, 95% CI 0.31-2.00, p=0.605; mod-severe vs. not severe SF: OR 0.66, 95% CI 0.33-1.33, p=0.244].

Conclusion: In summary, the results of this *post-hoc* analysis suggest that PROs in CD, AP and SF, do not provide prognostic information on the likelihood of clinical or endoscopic response. These findings question whether PROs should be relied upon for defining inclusion criteria or evaluating outcomes of patients in clinical trials of CD. Composite scores that include both subjective PROs in combination with objective findings from endoscopy, C-reactive protein or fecal calprotectin should be evaluated as predictive tools for clinical and endoscopic outcomes.

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Introduction: Tofacitinib has shown promising results in ulcerative colitis (UC) in the pivotal trials (OCTAVE) that should be confirmed in clinical practice.

Aims & Methods: Our aim was to evaluate the effectiveness and safety of tofacitinib in UC in real life. Patients from the prospectively maintained ENEIDA registry treated with tofacitinib due to active UC [Partial Mayo Score (PMS) ≥ 2 points] were included. Clinical activity and effectiveness were defined based on PMS. Short-term response was assessed at week 4, 8 and 16. Last-observation-carried-forward method was used in patients that stopped tofacitinib before the time-points for clinical assessment. Variables associated with short-term remission at week 8 were identified by logistic regression analysis. The cumulative retention rate and the cumulative incidence of relapse over time were assessed by survival curves. Cox-regression analysis was performed to identify predictive factors of tofacitinib discontinuation or relapse over time. Data quality was assessed by remote monitoring.

Results: 113 patients were included and exposed to tofacitinib a median of 44 weeks [interquartile range (IQR)=30-66]. Seventy percent of them had extensive colitis, median PMS at baseline was 6 (IQR=6-8), 86% had C-reactive protein over the upper limit. One hundred percent of patients had been exposed to anti-TNF, 89% to vedolizumab and 4% to ustekinumab. Sixty nine percent of patients had received ≥ 3 biologics, and 11% were on concomitant immunomodulators. Response and remission at week 8 were 60% and 31%, respectively. In multivariate analysis, higher PMS at week 4 [odds ratio (OR)=0.2; 95% confidence interval (CI)=0.1-0.4] was the only variable associated with the likeliness (lower) of achieving remission at week 8. Higher PMS at week 4 (OR=0.5; 95%CI=0.3-0.7) and higher PMS at week 8 (OR=0.2; 95%CI=0.1-0.5) were associated with lower probability of achieving remission at week 16. 20% of those without remission at week 4, and 12% of those without remission at week 8, achieved remission at week 16. A total of 45 patients (40%) discontinued tofacitinib over time; discontinuation rate was 34% and 46% at 24 and 52 weeks, respectively. The reasons for tofacitinib discontinuation were: primary non-response in 29 patients (26%), adverse events in 7 patients (6%), relapse in 6 patients (5%), partial response in 2 patients (2%) and pregnancy wish in 1 patient (1%). PMS at week 8 was the only factor associated with tofacitinib discontinuation [Hazard ratio (HR)=1.5; 95%CI=1.3-1.6].

A total of 34 patients had remission at week 8; from them, 65% relapsed 52 weeks after achieving remission; 9 patients increased the dose to 10 mg/12 h and 5 reached remission again. No factors associated with relapse over time were identified. 18 patients had adverse events (4 hypercholesterolemia, 2 herpes zoster, 3 infections, 2 dyspnea, 1 neoplasia, 1 lymphopenia, 1 headache, 1 hypertriglyceridemia and 4 others). No thromboembolic events were reported.

Conclusion: Tofacitinib is relatively effective in UC patients in real practice even in a highly refractory cohort. Only 10% of the patients without remission at week 8 reached remission at week 16. A relevant proportion of patients discontinued the drug over time, mainly due to primary failure. Over 60% of patients that achieve remission, relapse over time, and about 50% regained response after dosage optimization. Safety was consistent with the known profile of tofacitinib.

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P0525

INFLUENCE OF THE INTERVAL OF TIME BETWEEN ANTI-TNF AND VEDOLIZUMAB OR USTEKINUMAB IN THE RESPONSE TO TREATMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: There is no evidence about the time that it is reasonable to wait until starting Vedolizumab (VDZ) or Ustekinumab (UST) in case of loss of response to anti-TNF therapy.

Aims & Methods: The aim of our study was to evaluate whether the time between the change from any anti TNF drug to VDZ or UST had an influence on the risk of treatment failure and the rate of adverse events or severe infections.

A retrospective, observational single-center study was designed. Inclusion criteria were all adult patients with moderate-to-severe IBD who started treatment with VDZ or UST due to loss of response to anti-TNF (Infliximab or Adalimumab). Exclusion criteria were patients who had received treatment for different indications such as prevention of recurrence or extra-intestinal manifestations. Patients that changed directly from VDZ to UST or from UST to VDZ were also excluded. We defined two groups of periods based on the interval of time between the last dose of anti-TNF and the first dose of VDZ or UST: Group A: early (≤ 30 days), Group B: late (31-60 days). Patients that had a waiting time of over 60 days were also excluded. Treatment failure after the initiation of VDZ or UST was defined as the need for dose intensification, surgical resection, therapy removal for ineffectiveness or adverse reaction. The existence of infections was also evaluated. Results are shown as percentages, median, range and Hazard Ratio (CI 95%). Fisher test and Cox Regression analysis were also performed.

Results: 46 patients (45.6% CD) were consecutively included (mean age 47.6 years). 52.2% were no smokers. 17 had initially been treated with Infliximab and 29 with Adalimumab. 21.7% were anti-TNF naïve and 78.3% had previously received 1 anti-TNF. The median of fecal calprotectin and C-reactive protein at the moment of drug change was 832 (range 172-1470) and 1.34 (range 0.42-1.98), respectively. 30 patients were changed to VDZ and 16 to UST. 23 patients were included in Group A and 23 in Group B. Treatment failure was observed in 20 patients: 9/23 in group A and 11/23 in group B with a median follow-up of 323 days (range 152-432). The reasons for treatment failure were dose intensification in 16 patients, surgery in 1 patient, adverse event in 1 patient and primary no response in 2 patients. 17 out of 30 patients on VDZ and 3 out of 16 on UST failed. The duration of the interval of time between stopping anti-TNF and starting VDZ or UST was not associated with increased risk of treatment failure ($p=0.25$). Median of time until loss of response was 252 days (range 98-432 days) in Group A and 168 days (range 131-418 days) in group B.

No differences were found between patients with CD or UC ($p=0.23$) nor in starting with VDZ or UST ($p=0.37$). There was one adverse event in group A which forced to stop treatment. No infections that required hospitalization were observed.

Conclusion: The interval of time between stopping anti-TNF and initiating VDZ or UST had no influence on the rates of treatment failure, adverse events or infections in our cohort.

Disclosure: Nothing to disclose

P0526

QUALITY OF LIFE OUTCOMES FROM PURSUIT-M TRIAL FURTHER SUPPORT EARLY DOSE OPTIMIZATION OF GOLIMUMAB IN MODERATE-TO-SEVERE ACTIVE ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is a chronic inflammatory disease that has the potential to negatively impact a patient's quality of life. Previously reported results from the phase 3 PURSUIT-M trial¹ in patients with moderate-to-severe active UC have shown that early dose optimization (EDO) of golimumab (GLM) in nonresponders to induction treatment can induce late pharmacokinetic and clinical response, with long-term clinical benefit.² Here, we evaluated the impact of EDO on patient-reported quality of life (QoL) outcomes among UC patients treated with GLM in the PURSUIT-M trial.

Aims & Methods: Patients with moderate-to-severe active UC were eligible for enrollment in the PURSUIT-M trial after completing the PURSUIT-SC³ or -IV⁴ induction trials. The PURSUIT-M maintenance trial included 456 early responders and 398 early nonresponders after excluding noncompliant subjects. At Week 6, participants who had responded to GLM induction (early responders) were randomized to receive maintenance with SC GLM 50 mg, 100 mg, or placebo every 4 weeks through to Week 60. Early nonresponders to GLM induction (N = 398) received maintenance with SC GLM 100 mg every 4 weeks from Week 6 through Week 60; those who achieved a clinical response at Week 14 are referred to as late responders. The primary endpoint was continuous clinical response to GLM or placebo maintenance without treatment failure. The Inflammatory Bowel Disease Questionnaire (IBDQ) was included as a secondary QoL endpoint. A descriptive analysis was performed and clinically significant improvement in IBDQ was defined as an increase of 20 points⁵ since baseline induction.

Results: The mean ages among early responders and late responders were relatively similar (39-41 years). Males were more frequently late responders (68%) than early responders (48-58%). Late responders had a higher mean Mayo score (9.3) than early responders (8.2-8.5). In early responders, compared with placebo, there was an increase in the percentage of patients who had a clinically significant improvement (>20-point increase) from induction baseline in IBDQ score with GLM maintenance (50 mg and 100 mg) at Week 6, which was sustained through Week 60 (table). At Week 60, 42.4% and 43.7% of early responders on GLM 50 mg and 100 mg, respectively, had a clinically significant increase in IBDQ score compared to 26.6% on placebo. In addition, at Week 60, 50% of late responders on 100 mg GLM maintenance had a clinically significant increase in IBDQ score compared to early responders on GLM 50 mg (42.4%) and 100 mg (43.7%). At least half of the late responders achieved a clinically significant increase in IBDQ score at Week 36 and 60 (table).

	Early (Week 6) Responders	Late (Week 14) Responders GLM 100 mg Maintenance			
	Placebo Maintenance	GLM 50 mg Maintenance	GLM 100 mg Maintenance	Yes	No
	N = 154	N = 151	N = 151	N = 112	N = 286
Mean (SD) IBDQ score at induction baseline	135.6 (33.3)	128.1 (33.2)	130.7 (32.8)	125.5 (34.6)	130.2 (32.0)
Subjects with a clinically significant increase from induction baseline in IBDQ score of >20 points ^a , n(%)					
Week 6 ^b	108 (70.1)	128 (84.8)	115 (76.2)	48 (42.9)	59 (20.6)
Week 36 ^b	53 (34.4)	77 (51.0)	74 (49.0)	65 (58.0)	82 (28.7)
Week 60 ^b	41 (26.6)	64 (42.4)	66 (43.7)	56 (50.0)	70 (24.5)

^aDefinition of clinically significant increase was based on the study of Irvine et al.⁵

^bSubjects who had a prohibited change in UC medication, an ostomy, colectomy, dose adjustment or discontinued study agent due to lack of therapeutic effect prior Week 60, were considered to have had no improvement in IBDQ. Subjects with a missing IBDQ value at Week 6, Week 36, or Week 60, were considered to have had no improvement in IBDQ at the respective timepoint.

[Table]

Conclusion: In this secondary analysis of the PURSUIT-M trial, participants treated with GLM maintenance had a clinically significant improvement in IBDQ score compared with placebo, which was maintained through Week 60. Nonresponders at Week 6 who became late (Week 14) responders on maintenance with GLM 100 mg had an IBDQ score profile at Weeks 36 and 60 that was similar to those of early responders receiving maintenance with GLM 50 mg and 100 mg. Consistent with efficacy benefits of EDO previously reported, these QoL findings further support EDO with GLM 100 mg maintenance dose on QoL.

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Disclosure: All authors are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA and may hold stock or stock options in the company.

P0527

EFFECTS OF OZANIMOD ON CIRCULATING LYMPHOCYTES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: FLOW CYTOMETRY RESULTS FROM THE STEPSTONE PHASE 2 STUDY

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Introduction: Ozanimod, an oral sphingosine 1-phosphate receptor modulator that selectively binds to receptor subtypes 1 and 5 with high affinity, decreases circulating T lymphocytes in animal models (Scott Br

J Pharmacol. 2016). A 12-week, open-label, multicentre, phase 2 study (STEPSTONE) evaluated ozanimod in patients with moderately to severely active Crohn's disease (CD); we report the effects of ozanimod on circulating lymphocytes and T cell subsets from this study.

Aims & Methods: Patients with CD (n=69, aged 19-70 years) received ozanimod 1 mg orally daily for 12 weeks. Multicolor flow analysis using Becton Dickinson FACSCanto II was performed by Q2 on blood samples collected on Day 1 (prior to treatment) and at Week 12. T- and B-lymphocyte subsets were assayed to quantify changes in absolute counts (Table). A T cell panel evaluated 11 subtypes: CD4+ naïve, T-helper (Th) 1 (Th1), Th1/Th17, Th2, Th17, CD4+ effector memory (EM), CD4+ central memory (CM), CD8+ terminally differentiated effector memory RA (TEMRA), CD8+ naïve, CD8+ EM, and CD8+ CM cells. Differences between Day 1 and Week 12 samples were analyzed by Wilcoxon signed rank tests. Flow cytometry was performed by Q2; Covance provided statistical analysis.

Results: At week 12, reductions in absolute total T cell, Th cell, Tc cell, and total B cell counts from the peripheral blood lymphocyte pool were observed (Table). Although both CD4+ and CD8+ T cells decreased with ozanimod treatment, a greater proportion of CD4+ T cells were affected, resulting in a higher proportion of CD8+ T cells in the peripheral blood lymphocyte pool. At week 12, reductions in CD4+ and CD8+ naïve, Th1, Th1/Th17, Th2, Th17, CD4+ and CD8+ EM, and CD4+ and CD8+ CM T cells were observed ($P < 0.001$); CD8+ TEMRA cells were largely unaffected.

Conclusion: Ozanimod resulted in a differential decrease in circulating lymphocytes, with reductions in total T cell, Th cell, and Tc cell counts, as well as all B cell subsets; however, NK cells and monocytes were not affected. T cell subtypes were not completely inhibited, and CD8+ TEMRA cells were largely unaffected. Findings suggest that, despite overall reductions in lymphocyte subsets relevant to the pathophysiology of CD, key subsets involved with immune surveillance are not significantly reduced with ozanimod treatment, and immune surveillance may remain intact. These findings are generally consistent with clinical safety results demonstrating a low risk of infection or malignancy in STEPSTONE (Feagan *Lancet Gastroenterol Hepatol.* 2020) and in patients with relapsing multiple sclerosis (Cohen *Lancet Neurol.* 2019; Comi *Lancet Neurol.* 2019).

	N	Median Day 1	Median Week 12	Median % Change	P value
Total T cell (CD3+)	45	1310	440	-66.0	<.0001
Th cell (CD3+CD4+)	42	759	160	-76.8	<.0001
Tc (cytotoxic) cell (CD3+CD8+)	42	456	273	-45.4	<.0001
B cell (CD3-CD19+)	41	223	38	-76.7	<.0001
Memory B	40	19.5	4.5	-78.0	<.0001
Double Negative Memory B	40	7.0	2.0	-71.4	<.0001
Non-switched Memory B	36	11.5	3.0	-80.0	<.0001
Naïve B	40	127	25	-75.6	<.0001
Plasmablast	32	3.0	1.0	-81.7	<.0001
Natural killer (NK) cell (CD3-CD56+/CD16+)	42	194	214	4.1	0.6403
Monocyte (CD14+)	41	545	490	-1.3	0.7215

[Table]

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P0528

EFFECTIVENESS AND SAFETY OF USTEKINUMAB IN ULCERATIVE COLITIS: REAL WORLD EVIDENCE FROM ENEIDA REGISTRY

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Introduction: Ustekinumab has shown promising results in ulcerative colitis (UC) in the development program (UNIFI) that should be confirmed in clinical practice.

Aims & Methods: Our aim was to evaluate the effectiveness and safety of ustekinumab in UC in real life. Patients included in the prospectively maintained ENEIDA registry that received at least 1 dose of ustekinumab intravenously due to active UC [Partial Mayo Score (PMS) ≥ 2] were included. Clinical activity and effectiveness were defined based on PMS. Short-term response was assessed at week 8 and 16. Last-observation-carried-for-

ward method was used in patients that stopped ustekinumab treatment before week 8 or 16. Variables associated with short-term remission were identified by logistic regression analysis. Data quality was assessed by remote monitoring.

Results: Forty-seven patients were included. Fifty-three percent had extensive colitis and 45% left-sided colitis. Median PMS was 6 (interquartile range=6-8). Thirty-one patients had endoscopic examination at baseline; 77% had severe activity. C-reactive protein was elevated in 79% of patients. All of the patients had been previously exposed to anti-TNF agents (70% to >2), 83% to vedolizumab and 26% to tofacitinib. Twenty-six percent of patients were under concomitant immunomodulators and 60% were receiving steroids at baseline. A total of 17 patients (36%) had response at week 8 [3 of them (6%) had remission]; 16 patients (34%) had response at week 16 [5 of them (11%) had remission]. There was a statistically significant decrease in CRP concentration during the induction only in patients with response at week 16. The proportion of patients with CRP elevated at baseline and at week 8 was higher among non-responders at week 16 (table 1). In the multivariate analysis, higher PMS at week 8 [odds ratio (OR)=0.5; 95% confidence interval (CI)=0.3-0.9] and CRP over the upper normal limit at week 8 (OR=0.1; 95%CI=0.01-0.8) were associated with lower probability of response at week 16; steroids during induction increased the probability of response at week 16 (OR=8; 95%CI=1-71). Of patients without response at week 8, only 7% achieved response at week 16. Seventeen out of 31 patients continued ustekinumab beyond week 16, despite being non-responders. Of these 17 patients, 4 reached remission after the 3rd dose, 1 after the 5th and 1 after the 7th one. There were 2 infections, one of them with fatal consequences (in a patient under steroids and tacrolimus due to renal transplant).

Conclusion: Ustekinumab shows benefit in some UC patients in real practice, even in a very refractory cohort in which the drug was prescribed as last resort. Patient status at week 8 seems to be a good predictor of response after the induction. Safety was consistent with the known profile of ustekinumab.

Variables	Non-responders	Responders	p
Female gender, n (%)	56	55	N.S.
Extensive colitis (%)	52	56	N.S.
Extraintestinal manifestations, n (%)	27	44	N.S.
Median partial Mayo score at baseline	6	8	0.03
Median partial Mayo score at week 8	3	2	0.03
Endoscopic severe activity (%)	84	67	N.S.
CRP upper the normal limit at baseline (%)	87	63	0.05
CRP upper the normal limit at week 8 (%)	67	31	0.02
Anaemia at baseline (%)	61	38	N.S.
Prior treatment with tofacitinib (%)	32	13	N.S.
Mean number of prior biologic agents	3	3	N.S.
Concomitant immunosuppressants, n (%)	19	38	N.S.
Steroids during induction, n (%)	57	43	N.S.

CRP, C-reactive protein; N.S., non-statistically significant

[Table 1. Characteristics of the study population based on the response to ustekinumab at week 16.]

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P0529

ANTI-USTEKINUMAB ANTIBODIES USING A DRUG TOLERANT ASSAY IS THE ONLY PREDICTIVE FACTOR OF CLINICAL REMISSION IN INFLAMMATORY BOWEL DISEASE PATIENT UNDER USTEKINUMAB

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Introduction: Ustekinumab (UST) is a human monoclonal antibody raised against IL 12 and IL 23, used for the treatment of inflammatory bowel diseases (IBD). The monitoring of this treatment is still unclear and need to be defined for patient optimization. Majority of published studies showed a low ustekinumab immunogenicity with no impact for clinical efficacy. This study aimed to bring out the relationship between ustekinumab blood concentration (USTC) and anti-ustekinumab antibodies measured by a drug tolerant assay using anti-human lambda chain for the detection of anti-drug antibodies (AUA) on one hand and the clinical response to the treatment by ustekinumab on the other hand.

Aims & Methods: USTC and drug-sensitive anti-UST antibodies were measured by Theradiag Lisa tracker® immunoassays during consultation. We included all patients that received UST and had USTC test from the first September 2016 to the 30th April 2019. Moreover, AUA were measured by drug-tolerant ELISA assay after patient's inclusion followed in our IBD center. Blood donors were used to define a threshold value of AUA. So, 21 wild samples from the French blood bank were measured using the drug tolerant assay to define a threshold value, adding two standard deviations to the mean. After uni- and bivariate analysis, a multivariate analysis using a mixed effects model of the clinical response according to CRP, smoking status, perineal lesion, serum albumin, previous use of vedolizumab, number of previous anti-TNFα drugs, and either the USTC or the AUA is done. A Spearman rank correlation was used to state relationship between USTC and AUA.

Results: We collected 138 blood samples from 56 IBD patients. Median age of patients was 39 years [31,8-44] and they were females in majority (69%). Forty-six percent smoked. Six had ulcerative colitis and the others had Crohn's disease with median Albumin levels over 40 g/L (43.1 [40,5-46,2]) and CRP levels under 10 mg/L (2,2 [0,8-5]). Sixty-nine percent of patient (n=37) were in clinical remission. The threshold value of AUA in the blood donors was defined as 11 µg/mL. In the 56 IBD patients, one sample was positive for detecting AUA in drug-sensitive assay vs 34 for drug-tolerant assay. In multivariate analysis, AUA using drug tolerant assay whatever titers was statistically significantly associated to the clinical remission (OR=0.3, IC 95% [4,30.10⁻¹⁶;5,56.10⁻¹], p=0.00562), but not USTC (OR 1.1, p=0.74). Using the threshold value isolated in blood donors, AUA over 11 µg/mL was also strongly associated to the clinical remission (OR 0.2, IC 95% [6,75.10⁻³;9,50.10⁻¹], p=0.0224). Correlation coefficient test between USTC and AUA was significant but low (r: -0.35, p=0.0002).

Conclusion: This is the first study showing that the presence of anti-ustekinumab antibodies (AUA) measured by a drug-tolerant assay was strongly predictive to clinical remission. Conversely, USTC was not significantly linked to the clinical remission. These data should be very important in the future to optimize our therapeutic strategies.

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Disclosure: Nothing to disclose

P0530

CORTICOSTEROID USE AND THE ASSOCIATED IMPACT ON PATIENTS WITH CROHN'S DISEASE (CD) AND ULCERATIVE COLITIS (UC) IN THE US, FRANCE, GERMANY, ITALY, SPAIN, AND UK (EU5)

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Introduction: Corticosteroids are an effective short-term therapy in inducing remission in patients with CD and UC. However, long-term and high dose corticosteroid use poses risk of serious side effects and complications.

Aims & Methods: This study assessed the impact of corticosteroid use and dose escalation on health-related quality of life (HRQoL) and work productivity and activity impairment (WPAI) amongst CD and UC populations in the US and EU5. This was a cross-sectional study among CD and UC patients and their gastroenterologists in the US and EU5. Data collected from two waves (Nov 2014 - Mar 2015 and Sep 2017 - Jan 2018) were merged. Physicians completed patient record forms (PRFs) for their next 8 CD and 7 UC patients, collecting data on diagnosis, management, treatment history and clinical outcomes. These same patients completed patient self-completion (PSC) forms, including patient reported outcomes measures assessing humanistic burden (HRQoL). Chi Squared and Kruskal Wallis analysis were used to compare demographics and treatment between no corticosteroid (NCS) patients vs lower dose (< 40mg/day) corticosteroid (LCS) and high dose (≥40mg/day) corticosteroid (HCS) patients. Linear regression analyses were conducted on the same groups to determine impact of corticosteroid and dose on patient-centered outcomes, using NCS as the reference category. Regressions were adjusted for age, time since diagnosis, severity at corticosteroid initiation, current flare status and biologic use. Sample base sizes vary due to patient self-completion variability.

Results: Data were extracted from 5725 CD PRFs, 2402 PSCs and 4980 UC PRFs, 2052 PSCs and stratified in accordance with current corticosteroid use and dose.

Patients using corticosteroids were younger (mean age: NCS: CD 40, UC 42; LCS: CD 39, UC 40; HCS: CD 37, UC 36) and were less likely to be prescribed biologics (NCS CD 53%, UC 41%; LCS CD 23%, UC 21%; HCS CD 24%, UC 20%) or immunomodulators (NCS: CD 38%, UC 34%; LCS: CD 32%, UC 28%; HCS: CD 33%, UC 29%). LCS patients had been receiving corticosteroids for longer vs HCS patients (mean weeks on corticosteroid: LCS CD 24, UC 19; HCS CD 11, UC 7).

Significant worsening in HRQoL, as measured by the EQ5D and SIBDQ, and WPAI was observed amongst CD and UC LCS and HCS patients (Table 1).

Conclusion: Corticosteroid use was significantly associated with worsened HRQoL and reduced work productivity amongst CD and UC patients. Greatest impact was observed amongst high dose cohorts, however worsened outcomes were also evident in the lower dose corticosteroid group where patients had been on corticosteroids the longest. There is a clear need for corticosteroid-sparing maintenance therapy in both CD and UC.

	LCS vs NCS		HCS vs NCS		R ²
	Coefficient [95% CI]	P value	Coefficient [95% CI]	P value	
CD (Patient reported)					
EQ5D (n=1791)	-0.02 [-0.04, -0.06]	0.011	-0.03 [-0.07, 0.00]	0.052	0.10
SIBDQ (n=1739)	-0.62 [-0.76, -0.48]	<0.001	-1.05 [-1.30, -0.80]	<0.001	0.22
WPAI (n=937)	5.34 [1.32, 9.37]	0.009	12.58 [1.32, 9.37]	0.003	0.13
UC (Patient reported)					
EQ5D (n=1541)	-0.03 [-0.05, -0.01]	0.007	-0.09 [-0.12, -0.06]	<0.001	0.11
SIBDQ (n=1480)	-0.65 [-0.79, -0.51]	<0.001	-1.41 [-1.63, -1.18]	<0.001	0.28
WPAI (n=776)	7.53 [2.99, 12.06]	0.001	14.54 [6.68, 22.41]	<0.001	0.17

[Table 1: HRQoL and Work Productivity in lower and high dose corticosteroid patients vs non-corticosteroid patients]

Disclosure: Mirko V. Sikirica is an employee and shareholder of Johnson & Johnson. John Lynch is an employee of Janssen Research & Development. Ben Hoskin, Jim Kershaw, Rosie Wild, and Rina Lukanova are employees of Adelphi Real World.

P0531

COMPARISON OF THE EFFICACY OF A SECOND INTRAVENOUS OR SUBCUTANEOUS ANTI-TNF IN THE TREATMENT OF ULCERATIVE COLITIS. REAL-WORLD DATA FROM THE ENEIDA REGISTRY

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Introduction: Three anti-TNFs (one intravenous and two subcutaneous) are currently licensed for the treatment of ulcerative colitis (UC). It is not known if the efficacy of a second anti-TNF changes on whether it is intravenous or subcutaneous; this could justify the indication of biological agents with a different mechanism of action in second line.

Aims & Methods: Aim: To compare the efficacy of a second subcutaneous or intravenous anti-TNF in UC patients naïve to other biological agents with different mechanisms of action.

Methods: Patients from the prospectively ENEIDA registry treated consecutively with intravenous and subcutaneous anti-TNF (or vice versa), who were naïve to other biological agents, were identified. Patients were classified according to the administration route of the first anti-TNF in: IVi (intravenous initially) or SCi (subcutaneous initially). Patients treated for extraintestinal manifestations or pouchitis were excluded. Clinical activity and effectiveness were defined based on Partial Mayo Score (PMS) at baseline, 14 and 52 weeks. Loss of response, dose-escalation and treatment discontinuation were also assessed.

Results: 468 UC patients were included (327 IVi & 141 SCi). Both cohorts were similar in clinical-epidemiological characteristics, except for a higher proportion of patients with moderate-to-severe clinical activity at the beginning of the first anti-TNF in the IVi group (81% vs. 69%; p=0.010) and at the beginning of the second anti-TNF in the SCi group (61% vs. 74%; p=0.007). Clinical response and remission rates at week 14 for the second anti-TNF were 43% and 31% in IVi vs. 49% and 27% in SCi, respectively (p=ns). At week 52, clinical response/remission rates of the second anti-TNF were 38%/33% in IVi vs. 41%/32% in SCi (p=ns). Higher clinical response and remission rates at 14 weeks with the second anti-TNF were detected in the SCi group (41% vs. 66%; p=0.008 and 26% vs. 50%, respectively; p=0.004) when the reason for withdrawal of the first anti-TNF was secondary loss of response. The cumulative persistence of the second anti-TNF treatment in IVi and SCi were 57% and 53% after 1 year, and 41% and 41% after 2 years, respectively (p=ns). The SCi group had lower rates of dose-escalation with the second anti-TNF than IVi (34% and 27% in SCi vs. 60% and 51% in EVi, at 12 and 24 months, respectively; p<0.0001). Globally, dose-escalation of the first anti-TNF and moderate-to-severe clinical activity at the beginning of the second anti-TNF were associated with a lower probability of remission with the second anti-TNF in the short and long-term.

Conclusion: In UC patients, the efficacy of infliximab after failure/intolerance of a subcutaneous anti-TNF is similar to that of subcutaneous anti-TNFs after infliximab failure/intolerance, suggesting that the type of anti-TNF used in the first line is not an issue when considering the need to change the mechanism of action in the second line of treatment.

Disclosure: Nothing to disclose

P0532

COMBINATION THERAPY IN IBD PATIENTS: DO WE NEED TO MAXIMIZE THE DOSE OF AZATHIOPRINE?

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Introduction: The use of combination therapy of anti-TNFα and thiopurines in Inflammatory Bowel Disease (IBD) is associated with greater efficacy and lower immunogenicity. However, the dose of thiopurine in this setting remains to be elucidated.

Aims & Methods: To compare the trough levels, anti-TNFα antibodies and the inflammatory biomarkers between 3 groups in combotherapy: group 1 (dose of azathioprine < 1mg/kg); group 2 (dose of azathioprine ≥ 1 and < 2mg/kg) and group 3 (dose of azathioprine ≥ 2mg/kg).

A retrospective study was performed, selecting all patients with established diagnosis of IBD, who were on combined maintenance treatment (at least 6 months of therapy) with azathioprine and anti-TNFα.

Results: We included 99 patients, 52.5% female with median age 33 (17-61) years. Eighty patients (80.8%) were diagnosed with Crohn's Disease and 19 (19.2%) with Ulcerative Colitis. Seventy-one (71.8%) patients were on infliximab (IFX) and 28 (28.3%) were on adalimumab (ADA). In patients treated with IFX, there were no differences in trough levels ($p=0.976$) or formation of antibodies anti-IFX ($p=0.478$) between groups. Moreover, there were no differences in inflammatory biomarkers: CRP ($p=0.385$) and fecal calprotectin ($p=0.576$) among the 3 groups. Regarding patients treated with ADA, there were no differences in trough levels of ADA ($p=0.249$), formation of antibodies anti-ADA ($p=0.706$) or in inflammatory biomarkers: CRP ($p=0.738$) and fecal calprotectin ($p=0.269$) among the 3 groups.

Conclusion: In our cohort there were no differences between anti-TNFα trough levels, formation of anti-TNFα antibodies or inflammatory biomarkers among patients in combotherapy with azathioprine, irrespective of its dosage. In conclusion, our study suggests that maintaining therapeutic levels of anti-TNFα drugs without antibodies formation is feasible with lower doses of azathioprine, minimizing its side effects.

Disclosure: Nothing to disclose

P0533

FECAL CALPROTECTIN AND DRUG LEVELS AT WEEK 14 PREDICT LONG-TERM RESPONSE OF VEDOLIZUMAB IN PAEDIATRIC INFLAMMATORY BOWEL DISEASES: A REPORT FROM THE PROSPECTIVE, MULTI-CENTRE VEDOKIDS STUDY

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Introduction: Limited data are available on the effectiveness of Vedolizumab (VDZ) in paediatric Crohn's Disease (CD) and Ulcerative Colitis (UC). We evaluated the effectiveness and safety of VDZ as well as prediction of response in an interim analysis of the prospective, multicenter VEDOKIDS study.

Aims & Methods: We enrolled children (age 0-18 years) with CD or UC commenced on VDZ with a standardized dosing of 177mg/BSA up to 300mg at 0, 2, 6 and q8 weeks thereafter. Non-responders had their dose escalated to q4wks at the discretion of the local physician. Explicit demographic, clinical and safety data were prospectively recorded via eCRF, as well as stool and serum samples at weeks 0, 14, 30 and 54. Clinical remission was defined as steroid and EEN-free remission (i.e. wPCDAI < 12.5 or PUCAI < 10) without the need for new medications. Complete remission was defined as clinical remission with CRP < 0.5mg/dL and ESR < 25mm/hr. Missing data were imputed for ITT analysis using the blended non-response imputation and LOCF approach. Fecal calprotectin (FC) was determined using the IDK ELISA Kit and serum VDZ drug using IDK monitor ELISA kit (both from Immundiagnostik AG Germany).

Results: Sixty-five children were enrolled, 33 (51%) with CD, and 32 (49%) with UC (29 (45%) males, 50 (77%) failed previous anti-TNF, median disease duration 2.6 years (IQR 1.4-5.3)). Twenty-three children (35%) discontinued the drug due to non-response ($n=19$ (29%)) or adverse events ($n=4$ (6.2%)). In addition, 6 children (18%) in the CD group and 2 (6.3%) in the UC group failed induction and their dose was escalated, none of whom achieved remission at week 54. Using the ITT principle, clinical remission rates for CD at weeks 14, 30 and 54 were 30%, 30% and 15%, respectively. Clinical remission rates at weeks 14, 30 and 54 did not differ between colonic and ileal disease, as well as B1 versus B2/B3 phenotype (all $p>0.05$). For UC the clinical remission rates at weeks 14, 30 and 54 were 41%, 47% and 47%, respectively (figure 1). Complete remission at week 54 was noted in four children (12%) in the CD group and ten (31%) in the UC group. Serum VDZ levels at week 14 (mean $10\pm9\mu\text{g/ml}$) correlated with fecal calprotectin levels at week 30 ($r=-0.51$, $p=0.03$). Three children (5%) had undetectable VDZ drug levels at week 54, none of whom in complete remission. FC at week 14 predicted complete remission at week 30 (mean FC levels $1467\pm744\mu\text{g/g}$ in non-responders vs $610\pm712\mu\text{g/g}$ in responders; $p=0.01$).

During the follow-up period, 76 adverse events were recorded in 39 children: 20 AEs were possibly related to VDZ, all of which mild-moderate and only 4 (20%) led to discontinuation of VDZ (Leukocytoclastic vasculitis, myalgia, dyspnea, fever and vomiting). There were 16 serious AEs, only one was graded as possibly related to VDZ (headache). There were 17 non-serious cases (28%) of upper respiratory infections (pharyngitis, tonsillitis, parotitis, and otitis media) and one *Campylobacter jejuni* which was graded as serious.

Conclusion: In this prospective multicenter study, VDZ was safe and effective in a refractory cohort of paediatric IBD, more so in UC. FC and drug levels post induction may predict longer term response.

Disclosure: This study is supported by grants from ECCO, ESPGHAN and Takeda Pharmaceuticals.

P0534

EFFICACY AND SAFETY OF USTEKINUMAB IN CROHN'S DISEASE: A REAL-WORLD STUDY FROM THE UNITED KINGDOM

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Introduction: Ustekinumab (UST), a human anti-IL12/23p40 monoclonal antibody, was approved in United Kingdom for the treatment of moderate to severe Crohn's disease (CD) in 2017 as has demonstrated effectiveness in clinical trials. Yet often, large international trial data does not concord with regional or even national experience.

Aims & Methods: This retrospective dual centre study aims to assess the efficacy and safety of Ustekinumab in a real-world, multi-ethnic and anti-TNF exposed CD cohort. All patients commenced on UST were included in the study from two sites of The University of Birmingham NHS Trust. Detailed data on demographics, previous treatment and disease phenotype were recorded. UST was given as an infusion (6mg/kg) at week 0 followed by 90mg subcutaneous injection at week 8 and 90mg SC every 8 weeks as maintenance. Clinical endpoints were 1) remission (Harvey Bradshaw Index (HBI) ≤ 4) 2) response (reduction in HBI of ≥3 or sustained HBI ≤4 points) at 12, 24 and 52 weeks. Adverse events were recorded.

Gender	Male	Female	30 (48%)	32 (52%)
Ethnicity	Caucasian	Asian Other	48 (78%)	12 (19%) 2 (3%)
Montreal Classification:				
Age at diagnosis, years:	A1 (<16)	A2 (16-40)	A3 (>40)	18 (29%) 38 (61%) 6 (10%)
Disease location:	L1 (Ileal)	L2 (Colonic)	L3 (Ileocolonic)	L4 (Isolated upper GI)
			19 (31%)	16 (26%) 27 (43%) 0
Disease behaviour:	B1 (Inflammatory)	B2 (Stricturing)	B3 (Penetrating)	25 (40%) 30 (49%) 7 (11%)
Perianal involvement:				
Total number of previous biologics:	1	2	3	Biologic naive
			16 (26%)	32 (52%) 12 (19%) 2 (3%)
Concomitant medications:	Thiopurine	Methodotrexate	16 (26%)	3 (5%)
Baseline data:	Mean HBI			9 (s.d. 4.08)

[Table 1. Baseline characteristics]

Results: 62 patients (Table 1) were included of whom 60 (97%) were biologic exposed and 44 (71%) had failed >1 previous biologic. 12-week clinical response was 69%, 24-week and 52-week remission rates were 52% and 69% respectively. 18 (29%) were on concurrent immunomodulation (IM). The 12-week response rate with concurrent IM was 78% versus 65% in non IM group.

Clinical remission was higher in those not on IM (56% not on IM versus 42% on IM). Clinical response rates were not significantly different in those with perianal disease versus without. Adverse events occurred in 8 (13%), 3 (5%) were considered major (suicidal ideation, severe headache, hypotension).

Disclosure: Nothing to disclose

P0535

SWITCHING FROM ORIGINATOR ADALIMUMAB (HUMIRA®) TO BIOSIMILAR (HULIO®) IN AN IBD POPULATION

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Introduction: Adalimumab (ADA) is administered subcutaneously and it has a systemic clearance of approximately 12 mL/hr. The mean terminal half-life is approximately 2 weeks (range: 10 - 20 days¹). Several studies have shown the effectiveness of infliximab biosimilars in IBD. However data regarding adalimumab biosimilars in IBD is lacking².

Aims & Methods: To assess clinical efficacy, safety and immunogenicity between adalimumab originator and adalimumab biosimilar (Hulio®) during a compulsory switch in an IBD population.

This was a prospective cohort study in which patients were assessed with validated clinical scores (CDAI for CD and SCCAI for UC), faecal calprotectin (FCP) and Adalimumab antibodies. Patients were reassessed 6 weeks post switch. A cut off FCP >250µg/g was used to determine active disease.

Results: Thirty three patients were recruited (F= 48%, mean age 38.5years; range 19-64 years). 81.8% had CD and 18.2% had UC. 18% had started ADA as their first anti-TNF due to patient preference for home injection. The rest (82%) had been previously on IFX and were switched due to loss of response (52%) or allergic reactions (48%).

There was no change in CDAI in 92% of patients pre and post switch, whilst 8% had an increase in their CDAI. There was no change in the SCCAI results in 80% of patients with UC patients, whilst there was a decrease in SCCAI in 20%.

There was no significant change in faecal calprotectin in the majority of patients (56.3%). In 18.7%, patients had a raised FCP >250µg/g pre and post switch, which remained elevated. 12.5% of CD patients had an improvement in their FCP to < 250µg/g and only 12.5% had an increase in their FCP >250µg/g post switch.

In the CD cohort, CDAI correlated well with FCP levels. In the patients with no CDAI change, 81% similarly had no change in their FCP levels. In the patients who had an increase in their CDAI scores post switch, 50% also had increase in their FCP levels, whereas 50% had no change in their normal FCP level.

In the UC cohort, SCCAI scores also correlated well with FCP levels with 100% of patients having compatible results. 75% of patients had no change in their clinical score, with all these patients having no change in their normal FCP level. In 25% there was a decrease in the SCCAI score which also had a decrease in the FCP level to < 250µg/g.

All patients had negative antibodies prior to switch and these remained negative post-switch.

9% stopped the biosimilar medication. This was due to an allergic reaction (33%) and uncontrolled disease activity (67%).

Conclusion: This prospective cohort study has shown a comparable clinical efficacy, safety and immunogenicity profile between adalimumab originator and biosimilar product.

The switching did not result in a clinically and biochemically significant difference in disease activity. Furthermore, there was a very good correlation between the FCP levels and clinical scores.

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Disclosure: Nothing to disclose

P0536

SYSTEMATIC REVIEW AND META-ANALYSIS: SAFETY OF VEDOLIZUMAB DURING PREGNANCY IN FEMALE PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab (VDZ) is a novel monoclonal antibody used in patients with inflammatory bowel disease (IBD). It is becoming prescribed more commonly, including in women of child-bearing age, due to its perceived safety profile, although data regarding outcomes for patients using VDZ during pregnancy are limited.

Aims & Methods: We performed a systematic literature search of MEDLINE, EMBASE and LILACS through January 2020 looking for studies including pregnancy outcomes in female patients with inflammatory bowel disease being treated with VDZ. Our primary outcome was a composite of adverse pregnancy-related events in female patients on VDZ compared to disease-matched controls on other medication regimens, including preterm births, early loss of pregnancy, late fetal death, elective termination of pregnancy and congenital anomalies.

Results: Four studies were included in our review, with three meeting criteria for our primary analysis. Compared to those who were VDZ naïve, those exposed to VDZ during pregnancy had no increase in overall adverse-pregnancy related outcomes (OR 1.43, 95% CI, 0.65-3.14). The VDZ group did have increased incidence of preterm births (OR 1.97, 95%CI, 1.10-3.54) but no difference in number of live births (OR 0.67, 95%CI, 0.38-1.18), early loss of pregnancies (OR 1.62, 95%CI, 0.90-2.91), or congenital malformations (OR 0.45, 95%CI, 0.05-3.83).

Conclusion: Our primary analysis supports the general safety of VDZ in pregnancy as measured by total adverse pregnancy events. We did identify an increased incidence of premature births with VDZ in our analysis, possibly confounded by disease activity, that needs to be examined in larger studies with less heterogeneity.

Disclosure: Nothing to disclose

P0537

BODY MASS INDEX DOES NOT IMPACT CLINICAL EFFICACY OF USTEKINUMAB IN CROHN'S DISEASE: A POST-HOC ANALYSIS OF THE IM-UNITI TRIAL

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Introduction: High body mass index (BMI) may be associated with increased risk of treatment failure in TNF-antagonist treated patients with inflammatory bowel disease. It is unclear if BMI has an impact on biologics with other mechanisms of action. This post-hoc analysis aimed to evaluate the impact of BMI on the efficacy of ustekinumab in the IM-UNITI study.

Aims & Methods: The impact of BMI on the efficacy of ustekinumab was evaluated using data from a 44-week maintenance study of ustekinumab (IM-UNITI, NCT01369355, YODA #2019-4105). Patients who had completed UNITI-1 and UNITI-2 and achieved clinical response by week 6 to ustekinumab were re-randomized to ustekinumab 90mg every 8 weeks, every 12 weeks, or placebo. The primary endpoint of IM-UNITI was clinical remission at week 44 (Crohn's disease activity index (CDAI) < 150). A key secondary endpoint of interest was corticosteroid-free (CSF) remission at week 44. Patients were stratified into the following subgroups, according to their BMI at study entry: normal < 25, overweight 25 - < 30, and obese ≥ 30. Chi-square test of linear trend was conducted for comparisons of frequencies between the three cohorts. Patients who did not complete all 44 weeks of the study or lost response and were offered open-label ustekinumab were considered non-remitters (intention-to-treat). Multivariate regression analyses evaluated possible association between BMI (as a categorical variable) and efficacy outcomes of clinical remission and CSF remission, with adjustment for variables found significant on univariate analyses. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Data was analyzed using Stata/IC 15.

Results: A total of 254 patients treated with ustekinumab were included in this analysis (5 patients omitted due to missing data). At week 44 of IM-UNITI, rates of clinical remission were numerically higher in those with normal BMI (57.2%; 83/145 patients) compared to overweight patients (45.1%; 32/71) and obese patients (55.3%; 21/38) (p=0.424), but not significant. There were similarly no significant differences observed when evaluating patients who received ustekinumab every 8 weeks only (normal BMI: 56.9% [41/72], overweight: 52.4% [22/42], obese: 58.8% [10/17]). Two variables were found significant on univariate analyses: baseline CRP < 3 (p=0.039) and baseline immunomodulator use (p=0.005). Multivariate logistic analysis did not find BMI was a significant predictor for clinical remission, when adjusted for co-variables. Obese or overweight patients had no difference in odds of attaining clinical remission at week 44 compared to patients with normal BMI (OR 1.09, 95% CI 0.64-1.86, p=0.753). Similarly, no significant differences were noted in odds of achieving CSF remission (overweight or obese vs. normal BMI [OR 1.21, 95% CI 0.71-2.06, p=0.485]). Ustekinumab drug level at week 44 was significantly lower in obese patients (median level 2.98 mcg/mL, IQR 2.86), as compared to patients who were overweight (4.84 mcg/mL, IQR 3.51)(p=0.021) or had normal BMI (4.43 mcg/mL, IQR 2.82)(p=0.014).

Conclusion: Although BMI impacts ustekinumab drug levels, there was no relationship of BMI on clinical efficacy. This may suggest that pharmacodynamic effects can be attained with approved doses of ustekinumab in patients with higher BMIs.

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P0538

EFFECTIVENESS OF THIRD-CLASS BIOLOGIC TREATMENT IN CROHN'S DISEASE: A MULTI-CENTER RETROSPECTIVE COHORT STUDY

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Introduction: Treatment options for patients with Crohn's disease (CD) have considerably increased in recent years with the advent of new biologics. Multiple studies described the effectiveness of ustekinumab (UST) and vedolizumab (VDZ) in CD patients failing anti-TNFs; however, the effectiveness of VDZ or UST as a third-class biologic has not yet been described.

Aims & Methods: The current study aims to investigate and compare the effectiveness of VDZ and UST as a third-class biologic in patients with CD. This was a retrospective multicenter cohort study. We included CD patients who received three different classes of biological therapy (anti-TNF, anti-integrin and anti-interleukin). The primary outcome was clinical response (≥ 3 reduction in Harvey-Bradshaw Index (HBI)) at week 16, and secondary outcomes were clinical remission (HBI ≤ 4), C-reactive protein (CRP)-normalization, adverse events, corticosteroid-free remission, and response at both week 16 and 52.

Results: One hundred sixty-five patients from 23 centers and 14 different countries were included in the study (48% male, mean age 44 (± 13) years, mean disease duration 18 ± 9 years; 41 patients were previously exposed to one, 108 to two, and 16 to three anti-TNF). 127 of 165 (77%) patients received VDZ as a second and UST as a 3rd class therapy (group A); the remaining 38 of 165 (23%) patients received UST as a second and VDZ as a 3rd class therapy (group B).

At week 16, 75/127 (59%) patients and 19/38 (50%) in groups A and B respectively responded to treatment ($p=0.323$); 36 out of 127 (28.3%) and 9 out of 38 (23.7%) were in clinical remission ($p=0.571$); 18/44 (40.9%) patients and 4/17 (23.5%) with elevated baseline CRP had normalized CRP

($p=0.679$); 12/55 (21.8%) and 5/17 (29.4%) patients treated with systemic corticosteroids at baseline achieved corticosteroid free-remission, respectively ($p=0.99$).

Forty seven out of the 165 patients had no available data at week 52; 63/91 (69.2%) patients, and 19/27 (70.3%) had responded to third class treatment in groups A and B, respectively ($p=0.613$); 30/91 (32.9%) and 4/27 (14.8%) were in clinical remission ($p=0.982$); 14/40 (35%) patients and 2/12 (16.7%) with elevated baseline CRP had normalized CRP, respectively ($p=0.227$).

Third class biologic was discontinued by 26/165 (15.75%) of the patients by the end of follow-up; 16/127 (12.5%) in group A and 10/38 (26.3%) in group B ($p=0.015$, hazard ratio 0.29 (95% CI 0.1-0.8) on multivariate Cox regression model). The reason for discontinuation of treatment was clinical failure in all patients excluding 4 for adverse events (arthralgia) and 2 for patient's decision.

Conclusion: The current study demonstrates that administering a third-class biological therapy is effective in more than half of the patients with CD, who have already failed two classes of biological drugs. No difference in effectiveness was detected between VDZ and UST as a 3rd class agent, however the rate of discontinuation was higher in patients that received VDZ after failure of UST. Further prospective studies are merited to evaluate the effectiveness of biologic sequencing strategies.

Disclosure: Nothing to disclose

P0539

ENDOSCOPIC AND HISTOLOGIC REMISSION IN TOFACITINIB TREATED REFRACTORY MODERATE-TO-SEVERE PATIENTS WITH ULCERATIVE COLITIS: A PROSPECTIVE REAL-LIFE COHORT

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Introduction: The pan-Janus kinase inhibitor tofacitinib (TFC) has recently been approved for treatment of moderate-to-severe ulcerative colitis (UC). Real-life data are limited, especially on endoscopic and histologic outcome. We report efficacy and safety of TFC in refractory UC patients, and assessed potential clinical predictors of response.

Aims & Methods: Thirty-five UC patients, all refractory to anti-TNF and vedolizumab, were prospectively included. All received TFC 10mg BID till week 8, and were endoscopically assessed at baseline (Mayo endoscopic sub-score ≥ 2) and week 8. Biological response was defined as a 50% decrease in faecal calprotectin (fCal) or fCal $< 250\text{mg/g}$, and biological remission as a fCal $< 250\text{mg/g}$ at week 8. Endoscopic response was defined as Mayo endoscopic sub-score of ≤ 1 , endoscopic remission as a sub-score of 0. Histologic remission was defined as a numeric Geboes score ≤ 6 (similar to $\leq 2A.0$). A non-response imputation and last observation carried forward analysis was applied.

Results: The Mayo endoscopic sub-score decreased significantly by week 8 ($p=0.004$), resulting in an endoscopic response and remission rate of 22.9% and 17.2% respectively. Histological remission was seen in 14.8% of

patients. Faecal calprotectin decreased from 1386mg/g down to 568mg/g by week 4 ($p=0.03$) (Table 2), but not further down by week 8 (703 mg/g, $p=0.5$) with a biological response and remission rate of 52.9% and 38.2%. Half of the patients with a PNR to one anti-TNF (10 out of 20) did discontinue TFC because of PNR. However, PNR to two anti-TNF agents almost exclusively (4 out of 5) resulted in PNR to TFC. In contrast, only 3 out of 8 vedolizumab PNR experienced PNR to TFC. Ultimately, 48.6% of all included patients discontinued TFC therapy after a median of 15.9 [12.4-26.6] weeks, all but one due to PNR, of whom 9/17 (52.9%) required colectomy. In multivariate analysis, a higher baseline albumin and a lower Mayo endoscopic sub-score were independent predictors of endoscopic (OR 1.06, $p=0.02$; OR 0.59, $p=0.003$) and biological remission (OR 1.06, $p=0.03$; OR 0.57, $p=0.01$). By week 8, creatinine kinase significantly increased ($p=0.001$), whereas the lipid profile was not significantly affected. One patient suffered from vaginal herpes infection, and one patient treated with TFC and high dose steroids developed disseminated nocardia, pneumocystic jiroveci, cutaneous zoster and varicella pneumoniae.

Conclusion: TFC can induce biologic, endoscopic and histologic remission in refractory UC, though clinical and predictive molecular markers are required to identify the right patients. In patients with prior PNR to 2 anti-TNF agents, TFC does not seem an alternative treatment strategy.

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P0540

PREDICTING TOFACITINIB INDUCED ENDOSCOPIC RESPONSE IN ULCERATIVE COLITIS THROUGH A MUCOSAL BIOMARKER

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Introduction: The pan-Janus kinase (JAK) inhibitor tofacitinib (TFC) has recently been approved for and added to the treatment armamentarium of patients with moderate-to-severe ulcerative colitis (UC). With increas-

ing choices and absence of predictive biomarkers generated from pivotal trials, real world data are needed to stratify patients based on their molecular fingerprint in order to improve likelihood of response.

Aims & Methods: We obtained inflamed colonic biopsies from 52 consecutive patients initiating biological therapy (anti-TNF [n=16], vedolizumab [VDZ, n=20]) or TFC [n=16] for active UC (Mayo endoscopic sub-score ≥ 2). Treatment choices were made in agreement between patient and physician, but all included patients were naïve for the mode of action initiated. All patients were treated with standard dosage according to the label. Response was defined as a Mayo endoscopic sub-score ≤ 1 and assessed by week 8-14. RNA was extracted and single-end RNA sequencing performed using Illumina HiSeq4000. Sequencing data were analysed through differential gene expression (DESeq2) and an unbiased network biology approach (Weighted Gene Coexpression Network Analysis).

Results: Response was observed in 5 (31.2%) anti-TNF, 13 (65.0%) VDZ, and 5 (31.2%) TFC treated patients. Previously reported markers for anti-TNF response, including *oncostatin M* (p=0.62), *TREM1* (p=0.70) and *IL13RA2* (p=1.0) could not differentiate TFC responders from non-responders. Similarly, the 4-gene vedolizumab signature [*MAATS1*, *PIWIL1*, *RGS13* and *DCHS2*] could not discriminate TFC responders from non-responders (p=0.13). No baseline differences in JAK/STAT-signaling could be identified either. Hence, we performed an unbiased network analysis of all TFC samples which identified 1 cluster of 65 genes, significantly correlating with response (p=0.006). The hub gene within this network turned out to be the most differentially expressed gene (p=1.5E-9, fold change [FC] 2.3), with a predictive accuracy for response of 100% (p< 0.001). In contrast, this gene could not predict anti-TNF or vedolizumab induced response (p=0.13; p=0.10 respectively). Of interest, baseline expression of the identified marker did not correlate with C-reactive protein, faecal calprotectin, Mayo endoscopic sub-score and other inflammatory markers including *IL-6*, *IL-1B* or epithelial markers. In TFC responders, the identified biomarker was significantly reduced by week 8, as compared to baseline (fold change [FC] -3.1, p=0.0004), but not in non-responders (FC 1.2, p=0.2).

Conclusion: We identified a TFC-specific biomarker unrelated to disease severity, increasing the potency of a robust predictive marker based on its underlying mode-of-action. Validation in independent larger datasets is warranted.

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P0541

CONTINUATION OF ANTI-TNF IN PATIENTS WITH ULCERATIVE COLITIS IN REMISSION IS NOT COST-EFFECTIVE COMPARED TO TREATMENT WITHDRAWAL: A MARKOV MODEL

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Introduction: Anti-tumor necrosis alpha (anti-TNF) treatment accounts for 31% of health care expenditures associated with ulcerative colitis (UC). Withdrawal of anti-TNF in patients with ulcerative colitis (UC) in remission may decrease risk of malignancies and infections, while promoting cost containment. Approximately 36% of patients will relapse within 12-24 months of anti-TNF withdrawal, but reintroduction of treatment is successful in 80% of patients. We aimed to evaluate the cost-effectiveness of continuation versus withdrawal of anti-TNF in patients with UC in remission.

Aims & Methods: We developed a Markov model comparing cost-effectiveness of anti-TNF continuation versus withdrawal. Transition probabilities were calculated from literature, or estimated by an expert panel of 11 gastroenterologists. Deterministic and probabilistic sensitivity analyses were performed to account for assumptions and uncertainty. The cost-effectiveness threshold was set at incremental cost-effectiveness ratio (ICER) of \$94,536 per quality-adjusted lifetime year (QALY).

Results: At 5 years, anti-TNF withdrawal was less costly (-\$12,772 per patient), but was also slightly less effective (-0.04 QALY per patient) than continued treatment. Continuation of anti-TNF compared to withdrawal resulted in an ICER of \$362,154/QALY, exceeding the cost-effectiveness threshold. Continued therapy would become cost-effective if the relapse rate following anti-TNF withdrawal was $\geq 44\%$ higher, or if adalimumab or infliximab (biosimilar) prices fell below \$102/40mg and \$76/100mg, respectively.

Conclusion: Continuation of anti-TNF in UC patients in remission is not cost-effective compared to withdrawal. A stop-and-reintroduction strategy is cost-saving but is slightly less effective than continued therapy. This strategy could be improved by identifying patients at increased risk of relapse.

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P0542

EARLY BIOMARKERS OF RESPONSE TO FERRIC CARBOXYMALTOSE TREATMENT IN GASTROINTESTINAL-RELATED INFLAMMATORY AND NON-INFLAMMATORY IRON DEFICIENCY ANEMIA: A PRELIMINARY STUDY

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Introduction: Iron deficiency anemia (IDA) is a frequent sign of several gastrointestinal diseases (GIDs) that requires to be managed efficiently. Oral iron formulations are often unsuccessful for inadequate absorption and poor compliance due to long duration of treatment and side effects. Ferric carboxymaltose (FCM) is a parenteral iron formulation which guarantees rapid resolution of IDA without need of repeated infusions. In clinical practice anemia resolution control is generally performed 12 weeks after FCM infusion, although it is not easy to predict which patients (pts) will not reach normal hemoglobin (Hb) levels.

Aims & Methods: The aim of the study was to highlight biomarkers of FCM treatment response that could early recognize patients (pts) who need re-infusion. The study included pts with GIDs-related IDA, not responding to oral iron therapy. On day 0, pts were treated with FCM per label dose, relative to individual Hb level and body weight. Full blood count and transferrin saturation index (TSI) were tested at baseline (T_0), after 4 weeks (T_4) and after 12 weeks (T_{12}) from FCM infusion. Ferritin was tested at T_0 and T_{12} . Based on resolution of anemia at T_{12} , namely Hb levels >13 g/dL for men and >12 g/dL for women, pts were divided in responders (R) and non-responders (NR). The cause of anemia was classified as inflammatory and non-inflammatory (including malabsorption and blood loss). Biomarkers evaluated were: age, sex, weight, ferritin T_0 , TSI T_4 and Δ TSI T_4 ($T_4 - T_0$). Parametric data are expressed as mean $\pm$ SD, non-parametric data as median (interquartile range) and relative statistical analysis between responders and non-responders was performed by Student's T-test and Mann-Whitney test respectively. Correlation was performed by Pearson's correlation coefficient. To assess the contribution of each predictor to FCM response, each biomarker was tested by univariate logistic regression analysis.

Results: 41 patients, 27 females (65.9%), mean age 63.5 ± 19.3 years and median weight 62 Kg (58-68.5) were enrolled in the study. 17 (41.5%) pts presented an inflammatory anemia. At T_{12} , resolution of anemia was observed in 29/41 pts (R 70.7%). Median Hb T_{12} was 13.5 g/dl (12.9-14) in responders and 11.1 g/dl (8.9-12.6) in non-responders. Response rate was independent of the cause of anemia ($p=0.5$). At T_0 , no differences were observed among sex, weight and TSI in the 2 groups of pts. Instead, age and ferritin resulted significantly lower in responders compared to non-responders ($p=0.018$ and $p=0.005$ respectively). At T_4 , TSI and Δ TSI resulted significantly higher in responders than in non-responders (TSI: R $22.2\% \pm 7.1$ vs NR $14.9\% \pm 7.1$, $p=0.012$; Δ TSI: R $16.5\% \pm 6.7$ vs NR $4.4\% \pm 10.5$, $p=0.002$). Both biomarkers resulted statistically correlated to Hb T_{12} : $r=0.49$ for TSI T_4 ($p=0.003$) and $r=0.62$ for Δ TSI T_4 ($p=0.0003$). The statistical significance of these two biomarkers was confirmed by the univariate analysis (TSI T_4 : $p=0.0079$ and Δ TSI T_4 : $p=0.0007$). ROC curve analysis was performed to select a cut-off value of response for both biomarkers. The most reliable biomarker of response resulted Δ TSI T_4 with a cut-off of $>9.2\%$ with sensitivity of 91.3% and specificity of 71.4% (AUC 0.842, 95%CI 0.663 to 0.9948, $p=0.0006$).

Conclusion: This pilot study showed that, 1 month after FCM infusion, Δ TSI resulted the best biomarker of FCM response in patients with GIDs-related IDA. Although its use should be validated in a larger multicenter study, Δ TSI T_4 might be used in clinical practice in order to avoid the delay of iron re-infusion in non-responders' patients.

Disclosure: Nothing to disclose

P0543

TOFACITINIB IN SEVERE STEROID RESISTANT ULCERATIVE COLITIS AS A RESCUE THERAPY

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Introduction: Despite the achievements of conservative treatment with biological drugs, to date, only infliximab refers to rescue therapy for severe steroid resistant ulcerative colitis (UC). In addition, up to 30% of these patients are the primary non-responders, and up to 20% lose response during the first year. Therefore it became necessary to study new alternative drugs with different pathophysiological mechanism such as tofacitinib as a rescue therapy.

Aims & Methods: 12 patients with clinical manifestations and endoscopic confirmation of severe steroid resistant UC are currently included in the prospective randomized study.

The mean age of the patients was 41 ± 5 years. All patients underwent clinical examination and bloodtests before the start of tofacitinib treatment, and on the 3, 5, 7, 10, 14 and 21 day of therapy. All patients received therapy with tofacitinib 20 mg daily during 8 weeks with further dose decrease to 10 mg daily. All patients underwent endoscopic examination after 12 weeks of treatment.

Results: At week 12 all patients showed a positive clinical and laboratory trend. Mean decrease of CRP was from 34,6 to 9,4 ($p < 0,05$) at day 5. Most patients (8/12, 66,6%) had stool frequency reduction $\sim 30\%$ from baseline and no blood seen (Mayo subscore 0) at day 5.

After 12 weeks 10 patients (83,3%) demonstrated remission or minimal endoscopic activity of the inflammatory process (Mayo subscore 0-1). 1 patient had moderate endoscopic activity, symptoms of moderate attack and was excluded from further observation. 1 patient had symptoms of mild attack and minimal endoscopic activity of the inflammation. In this patient dose was optimized to 20mg daily.

Conclusion: The results show that tofacitinib can be effective as a rescue therapy for severe steroid resistant UC, as well as a drug for achieving clinical and endoscopic remission.

Disclosure: Nothing to disclose

P0544

USE OF MYCOPHENOLATE MOFETIL IN INFLAMMATORY BOWEL DISEASE: RESULTS FROM THE ENEIDA REGISTRY

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Introduction: Mycophenolate mofetil (MMF) is an immunomodulatory drug that inhibits T and B cells, by reversible inhibition of inositol monophosphate dehydrogenase. MMF is commonly used for prophylaxis of organ rejection however studies to evaluate its use in inflammatory bowel disease (IBD) are limited especially after the appearance of biological treatments. The aim of this study was to evaluate the efficacy and safety in IBD patients.

Aims & Methods: Based on the ENEIDA registry (a large, prospectively maintained database of the Spanish Working Group in IBD—GETECCU), IBD patients that had received MMF were identified. Only IBD patients with an established diagnosis of Crohn's disease (CD) or Ulcerative colitis (UC) in whom oral MMF was prescribed for this condition (except for perianal disease) were evaluated. Demographic and IBD clinical data (time from diagnosis, IBD type and extension, concomitant treatments, steroids use) were collected. Clinical activity for Harvey-Bradshaw Index (HBI) and partial Mayo score (pMS), endoscopic activity, C reactive protein (CRP) and faecal calprotectin (FC) were reviewed at baseline (at MMF starting), 3 and

6 months and at final follow-up (at MMF stopping or last visit using MMF). Adverse events (AEs), surgeries and hospitalizations during MMF treatment were documented. Statistical analysis were performed by descriptive statistics and non-parametric tests.

Results: Between June 1999 and November 2018 a total of 83 patients received MMF for IBD treatment (mean age 36.4 (± 12.3) years; 52F/31M; 66 CD (L1 17,2%; L2 21,9%; L3 48,4%) and 17 UC (E1 11,8%; E2 29,4%; E3 58,8%)). Indication for MMF use were maintenance of remission (50%), induction of remission (43,6%) and postsurgical prophylaxis (6,4%). MMF therapy was initiated before 2010 in 59% of patients. Mean MMF dosis used was 1269.8 (± 741) mg/day. In 61% of cases, systemic steroids were administrated starting MMF and it was used concomitantly to biologic agents in 27.3% of patients (16 Infliximab/ 3 Adalimumab/ 1 Vedolizumab/ 1 Ustekinumab).

In CD patients, statistically significant differences in HBI at 6 months (mean 5.9 (SD 4.8), $p = 0.04$) and at the end of follow-up (mean 5.7 (SD 5), $p = 0.014$) compared with baseline (mean 7.6 (SD 4.3)) were observed. Alike in UC patients, statistically significant differences in pMayo score at 6 months (mean 2.1 (SD 2.7), $p = 0.018$) and at the end of follow-up (mean 1.8 (SD 2.6), $p = 0.003$) compared to baseline (mean 4.8 (SD 2.5)) were determined. No significant differences in PCR or CF values during follow-up were observed. Concomitant use of biologics was significantly associated with clinical response (OR 1.36 95% CI 1.08-1.73). Survival curve showing maintenance of MMF treatment (Figure 1). The drug was maintained for a median time of 28.9 months (20.4-37.5). MMF was stopped in 84% (68/83) of patients (50% due to lack of response, 16,7 % for loss of response and 15,3% for remission) and required hospitalization or surgery, during MMF treatment, in 26% and 9.9% of patients, respectively. A total of 22.8% (19/83) patients developed adverse events related to the MMF (60% abdominal pain). In 10.8% (9/83), these adverse events resulted in drug withdrawal.

Conclusion: Mycophenolate mofetil-MMF shows a clinical benefit in the long term both in UC and CD patients with a good safety profile. MMF could be a treatment option alone or in combination with biologics in patients with IBD in clinical practice.

Disclosure: Nothing to disclose

P0545

USE OF GASTRIC ACID SUPPRESSANTS AND RISK OF DISEASE ACTIVITY EXACERBATION IN ADULT PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Gastric acid suppressants such as proton pump inhibitors (PPI) and histamine 2 receptor antagonists (H2RA) are common gastrointestinal medications used to manage symptoms of acid related diseases. Studies have shown that these medications are associated with increased risk of pneumonia, vitamin deficiency, osteoporosis and fractures. Few studies have described the potential risk of inflammatory bowel disease (IBD) exacerbation among patients on gastric acid suppressants but little is known on its association.

Aims & Methods: This study aims to investigate the effect of the use of gastric acid suppressants (PPI and H2RA) in the risk of IBD (Crohn's disease and ulcerative colitis) exacerbation. A comprehensive, computerized literature search from the electronic database of MEDLINE, Google scholar, Cochrane Library, and OVID was performed with the following search terms:

gastric acid suppressants, proton pump inhibitors, histamine 2 receptor antagonists, inflammatory bowel disease, Crohn's disease, ulcerative colitis, outcomes, and disease activity exacerbation. Two cohort studies were selected and validated using the Newcastle-Ottawa criteria. Trial results were combined under a random effects model using pooled relative risks (RRs). The Cochrane Review Manager Software version 5.3 was used for all analyses.

Results: Two cohort studies comprising of 36,293 patients were analyzed. In the fixed effects model, the pooled RR of disease activity exacerbation with use of gastric acid suppressants in general was 1.20; 95% CI (1.16-1.23) and it exhibited statistical homogeneity ($I^2 = 0\%$). The effects of PPIs and H2RAs were also separately analyzed under the fixed effects model. The pooled RR of disease activity exacerbation with the use of PPIs was 1.18; 95% CI (1.14-1.22). The pooled RR of disease activity exacerbation with the use of H2RAs was 1.25; 95% CI (1.17-1.32). Both analyses also showed statistical homogeneity ($I^2 = 0\%$).

Conclusion: Use of gastric acid suppressants such as PPIs and H2RAs may be associated with increased risk of disease activity exacerbation in patients with IBD. This meta-analysis confirms the need for further prospective studies in examining this relationship.

Disclosure: Nothing to disclose

P0546

TOFACITINIB IN ACUTE SEVERE ULCERATIVE COLITIS: A REAL WORLD TERTIARY CENTRE EXPERIENCE

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Introduction: Tofacitinib is a Janus kinase inhibitor with proven efficacy in the treatment of moderate to severe ulcerative colitis (UC). However, real world data are limited and outcomes for using tofacitinib in hospitalised patients with severe UC are scarce^{1,2}.

Aims & Methods: The aim was to assess the outcomes of tofacitinib use in a series of biologic and steroid refractory patients admitted with an exacerbation of UC. A retrospective analysis was conducted of consecutive patients treated with tofacitinib in the inpatient setting at a tertiary inflammatory bowel disease referral centre between February 2019 to February 2020. The primary outcome was need for colectomy during admission and during follow up. Secondary outcomes included clinical response, remission and corticosteroid use post induction.

Results: Seven anti-TNF and steroid refractory patients received in-hospital tofacitinib at our institution; five met the criteria for acute severe UC. Baseline inpatient endoscopy showed severe colitis with a Mayo endoscopy sub-score of 3 and a mean ulcerative colitis endoscopic index of severity of 5.7. Following tofacitinib induction, there was a rapid and significant reduction of bloody stool frequency (range 2-7 days) alongside normalisation of CRP at the point of discharge in 5/7 patients. To date, 3/7 patients have avoided colectomy and are in steroid free clinical remission with significant improvement at post induction endoscopy (mucosal healing (Mayo 0-1) in 2 of 3 patients). Despite standard tofacitinib induction dosing throughout, four patients required subtotal colectomy; two during index admission and two following readmission within 90 days. No drug related adverse events were recorded.

Conclusion: This is the largest reported case series of tofacitinib effectiveness in hospitalised patients with severe colitis. Tofacitinib can be considered as a potential rescue agent in severe UC with our experience demonstrating avoidance of colectomy in three hospitalised anti-TNF and steroid refractory patients.

However, the failure rate of medical treatment is high in keeping with the remaining patients in our cohort eventually requiring referral for colectomy.

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P0547

IMPROVED WORK PRODUCTIVITY IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH MESALAZINE IN ROUTINE CLINICAL PRACTICE IN THE NETHERLANDS: RESULTS FROM THE IMPACT STUDY

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Introduction: Mesalazine is the first-line treatment for mild-to-moderate ulcerative colitis (UC), with high rates of efficacy in induction and maintenance of remission.^{1,2} UC can have a negative impact on work productivity, particularly during periods of active disease.^{3,4} Real-world evidence on how mesalazine can improve work productivity in patients with UC is currently limited.

Aims & Methods: IMPACT, a single arm, non-interventional, observational, prospective study, assessed mesalazine use in Dutch clinical practice. Adults with mild-to-moderate UC that extended beyond the rectum and who received prolonged-release mesalazine (as sachets of granules or tablets) for active disease were followed for 12 months; those who received additional treatments (local/systemic steroids, immunosuppressants, biologics) were excluded.

Time to dose reduction (TDR) was the primary outcome and work productivity a secondary outcome. Work productivity was assessed using the Work Productivity and Activity Impairment (WPAI) questionnaire⁵ at Visit 1 (baseline), Visit 4 (Month 3) and Visit 7 (Month 12 or at study drop out); including information on current employment (yes/no), average hours worked per week, hours of work missed in last 7 days due to problems associated with UC, and ratings of impact of UC on work productivity and

other daily activities (using scale of 0= no effect to 10= total prevention of activity). IMPACT was conducted in line with the Declaration of Helsinki and registered as NCT02261636.

Results: Of 151 patients (median age 46 years; UCDAI score: median 5.0, mean 5.4), 71.5% (108) were newly diagnosed with mild-to-moderate UC and the majority initiated on a daily dose of 4g as a sachet (115; 76.2%). Dose reductions occurred in 31.8% (48) of patients with the mean TDR being 8.3 months. Unemployment was relatively stable at 26-30% throughout the study as was the average hours worked per week (median 36 at all visits, mean 34.4-35.1) (Table). At Visit 4, patients showed a numerically strong reduction versus Visit 1 in mean weekly hours of work lost due to UC (1.4, standard deviation [SD 5.8] vs 5.4 [SD 11.4]), mean rating of impact of UC on work productivity (1.4 [SD 2.6] vs 3.6 [SD 3.4]), and mean rating of impact of UC on other daily activities (1.5 [SD 2.5] vs 4.0 [SD 3.4]). These improvements were maintained, albeit slightly lower (likely due to inclusion of data from patients with symptom flares that subsequently dropped out), through Visit 7 (mean hours of work lost: 2.7 [SD 8.1]; mean rating of impact on work productivity: 2.0 [SD 3.2]; mean rating of impact on other daily activities: 2.4 [SD 3.3]).

Conclusion: Patients with mild-to-moderate UC receiving daily mesalazine treatment (predominantly as 4g sachet) reported increased work productivity, which was maintained through 12 months of therapy.

Work productivity question	Visit 1	Visit 4	Visit 7
Currently employed, n (%)	110/151 (72.8%)	76/103 (73.8%)	85/122 (69.7%)
Mean weekly hours worked (standard deviation)	34.7 (11.8)	35.1 (11.9)	34.4 (12.4)
Median weekly hours worked (range)	36.0 (2-70)	36.0 (10-70)	36.0 (6-70)
Mean hours of work lost due to UC in last week (standard deviation)	5.4 (11.4)	1.4 (5.8)	2.7 (8.1)
Median hours of work lost due to UC in last week (range)	0.0 (0-44)	0.0 (0-32)	0.0 (0-40)
Mean rating of impact of UC on work productivity (standard deviation)	3.6 (3.4)	1.4 (2.6)	2.0 (3.2)
Median rating of impact of UC on work productivity (range)	3.0 (0-10)	0.0 (0-10)	0.0 (0-10)
Mean rating of impact of UC on other daily activities (standard deviation)	4.0 (3.4)	1.5 (2.5)	2.4 (3.3)
Median rating of impact of UC on other daily activities (range)	4.0 (0-10)	0.0 (0-8)	0.0 (0-10)

[Work productivity results]

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P0548

MEDICAL TREATMENT OF INFLAMMATORY BOWEL DISEASE DURING THE FIRST 12 MONTHS OF FOLLOW-UP IN PEDIATRIC, ADULT AND ELDERLY PATIENTS: A NORWEGIAN NATIONWIDE REGISTRY STUDY FROM 2009 TO 2016

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Introduction: Age of onset seems to influence the disease characteristics and clinical course in inflammatory bowel disease (IBD). A lower use of advanced medical therapies has been reported in late-onset IBD (>60 years). More real-world, population-based data on treatment of elderly IBD patients are needed. We performed a nationwide registry study to estimate the use of medical treatment in pediatric, adult and elderly onset IBD during the first 12 months of follow-up after diagnosis.

Aims & Methods: Data on all patients with an ICD-10 code registration (K50 or K51) in the Norwegian National Patient Registry between 2009 and 2016 were linked to the Norwegian Prescription Database. IBD cases were defined as ≥1 IBD hospital event and ≥2 IBD prescriptions. Patients with < 2 IBD prescriptions were included if they had ≥1 IBD hospital event for each year of follow-up. Date of diagnosis was set at first IBD hospital event, and medical treatment during the first 12 months of follow-up were retrieved. Age was only available as ten-year birth cohorts. Patients born after 1999 were classified as pediatric cases, patients born from 1950 to 1999 as adult cases and patients born before 1950 as elderly cases. Differences in proportions were calculated by chi-square test.

Results: A total of 14,704 incident IBD cases were included, 5,135 (35%) with Crohn's disease (CD) and 9,569 (65%) with ulcerative colitis (UC). There were 359 (7%) pediatric, 4,173 (81%) adult and 603 (12%) elderly CD cases. The respective numbers for UC were 225 (2%), 7,736 (81%) and 1,608 (17%). Main results are summarized in Table 1.

Medication	Total CD, n = 5135 (%)	Pediatric, n = 359 (%)	Adult, n = 4173 (%)	Elderly, n = 603 (%)	p
Biologics	1484 (29)	187 (52)	1251 (30)	46 (8)	<0.001
Steroids	3721 (72)	201 (56)	3059 (73)	461 (76)	<0.001
5-ASA	1721 (34)	150 (42)	1381 (33)	190 (32)	0.002
IMs	2279 (44)	307 (86)	1847 (44)	125 (21)	<0.001

Medication	Total UC, n = 9569 (%)	Pediatric, n = 225 (%)	Adult, n = 7736 (%)	Elderly, n = 1608 (%)	p
Biologics	936 (10)	59 (26)	814 (11)	63 (4)	<0.001
Steroids	5555 (58)	162 (72)	4435 (57)	958 (60)	<0.001
5-ASA	8761 (92)	210 (93)	7146 (92)	1405 (87)	<0.001
IMs	1388 (15)	119 (53)	1154 (15)	115 (7)	<0.001

[Table 1. Initiation of medical treatment after first 12 months of follow-up.]

Pediatric CD and UC cases received more biologics and immunomodulators (IMs, including methotrexate and thiopurines) than adult and elderly cases. Biologics and IMs were only used in a minority of elderly CD and UC cases. At least two thirds of elderly CD and UC cases received steroids, while pediatric CD cases had the lowest steroid use. Elderly cases had the lowest 5-aminosalicylic acid (5-ASA) use, although these proportions were similar to the pediatric and adult cases.

Conclusion: Biologics and IMs were only used in a minority of elderly cases as compared with pediatric and adult cases, and these findings are in line with previous reports. A lower use of biologics and IMs in late-onset

IBD could reflect a milder disease course or a more cautious treatment strategy in elderly patients. Differences in advanced medical treatment might have consequences regarding treatment outcome and surgery rates should be investigated.

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P0549

PERFUSE: A FRENCH PROSPECTIVE/RETROSPECTIVE NON-INTERVENTIONAL COHORT STUDY OF INFLIXIMAB-NAÏVE AND TRANSITIONED PATIENTS RECEIVING INFLIXIMAB BIOSIMILAR SB2; INTERIM ANALYSIS

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Introduction: SB2 is an EU-approved infliximab (IFX) biosimilar, having demonstrated bioequivalence and similar efficacy, safety and immunogenicity as the reference. Little evidence is published on long-term, real-world use of SB2 in patients who are either IFX-naïve or transitioned from originator or another IFX biosimilar. PERFUSE is an ongoing non-interventional study of 1374 patients receiving SB2 as routine therapy at 12 gastroenterology sites across France, designed to describe clinical characteristics, immunogenicity and SB2 persistence over 12 months.

Aims & Methods: To describe clinical characteristics, immunogenicity and treatment persistence over 12 months in patients initiating SB2 in routine clinical practice. Eligible adult patients have a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) and initiated SB2 in routine clinical practice after September 2017. Data are captured prospectively and/or retrospectively from patient records obtained during routine clinic visits for up to 12 months following initiation. Outcome measures include persistence on SB2, clinical characteristics at baseline (initiation of SB2), disease scores (Harvey-Bradshaw Index [HBI], Simple Clinical Colitis Activity Index [SCCAI]), and anti-IFX antibodies (ADA).

Results: This interim analysis (IA) includes 744 IBD patients: 570 with CD; 236 female, 57 IFX-naïve, 513 transitioned from prior IFX, and 174 with UC; 78 female, 32 IFX-naïve, 142 transitioned from prior IFX. In the 655 patients with prior IFX, no clinically relevant difference in disease score from baseline to Month 12 (M12) was observed; mean individual change was -0.3 (95% CI -0.7, 0.1) and -0.3 (95% CI -0.7, 0.1) in the CD cohort transitioned from reference IFX (n=184) and biosimilar IFX (n=100), respectively, and -0.5 (-1.1, 0.2) and 0.0 (-0.7, 0.8) in the UC cohort transitioned from reference IFX (n = 46) and biosimilar IFX (n = 35), respectively. Mean SB2 dose (mg/kg, SD) was similarly unchanged from baseline: 7.1 (2.4) and 7.2 (2.4) to M12: 7.7 (2.5) and 7.4 (2.4) in patients with CD transitioned from reference IFX or biosimilar IFX; 7.1 (2.4) and 7.4 (2.4) to 7.6 (2.5) and 7.4 (2.4) in patients with UC transitioned from reference IFX or biosimilar IFX, respectively. By data extract date, 451 patients with CD and 138 with UC had reached M12; persistence on SB2 was 93.1% (95% CI 90.4, 95.3) and 90.6%

(95% CI 84.4, 94.9) in CD and UC, respectively. Reasons for discontinuation (n) were: adverse event (8), primary loss of response (9), secondary loss of response (18) and unspecified (13). Serious adverse events were reported for 5 UC patients (TB, anal fistula, pouchitis, rash, allergic reaction) and 8 CD patients (abscess, subocclusive syndrome, rectal abscess, intestinal obstruction [4 patients], infectious diarrhoea).

	CD			UC		
	n	Mean (SD)	Q1, Q3	n	Mean (SD)	Q1, Q3
Age, years	570	38.6 (13.5)	28, 47	174	40.7 (13.8)	29, 50
Duration of disease		13.3 (9.3)	6, 19		9.5 (7.9)	4, 14
Prior IFX treatment	Naïve	57	-	-	32	-
	Originator	353	-	-	88	-
	Biosimilar	160	-	-	54	-
Mean SB2 dose (mg/kg)	At initiation	509	7.0 (2.4)	5, 10	155	7.0 (2.4)
	At M12	418	7.5 (2.5)	5, 10	125	7.5 (2.4)
	n	Mean (SD)	95% CI	n	Mean (SD)	95% CI
Patients remaining on SB2 at M12, n (%)	451	420 (93.1)	90.4, 95.3	138	125 (90.6)	84.4, 94.9
HBI (prior IFX only)	Baseline	358	2.3 (3.1)	2.0, 2.6	-	-
	M12	328	2.0 (2.4)	1.7, 2.3	-	-
	Individual change: M12-baseline	284	-0.3 (2.4)	-0.6, 0.0	-	-
SCCAI (prior IFX only)	Baseline	-	-	-	100	1.4 (2.0)
	M12	-	-	-	84	1.0 (1.7)
	Individual change: M12-baseline	-	-	-	81	-0.2 (2.2)
ADA, n ever tested, (positive at baseline; positive post-baseline)	IFX-naïve	20 (n/a; 2)	11 (n/a; 4)			
	IFX-prior	296 (24; 12)	86 (6; 4)			

[Table 1. Baseline characteristics, SB2 persistence, disease scores and immunogenicity]

Data extract date: 27th March 2020

Conclusion: This IA indicates that patients with IBD can be successfully transitioned from originator or biosimilar IFX to SB2, without loss of disease control, and with no immunogenicity or safety concerns. Over 90% of all patients continued on SB2 treatment at M12 post-initiation.

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P0550

USTEKINUMAB IMPROVES HEALTH-RELATED QUALITY-OF-LIFE IN PATIENTS WITH MODERATE-TO-SEVERE CROHN'S DISEASE: RESULTS FROM A WEEK 16 INTERIM ANALYSIS OF THE STARDUST TRIAL

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Introduction: A treat-to-target (T2T) strategy may optimize inflammatory bowel disease management. STARDUST is a randomized, interventional phase 3b study in Crohn's disease (CD) patients, evaluating endoscopic response to ustekinumab (UST) at 48 weeks. After 16 weeks of UST induction, 67% of the 500 patients enrolled reached clinical remission and 37% of patients randomized to the T2T arm (CD Activity Index [CAI] 70 responders) showed endoscopic response by central reading.¹ Here we describe the health-related quality of life (HRQoL) response to UST induction at 16 weeks from the interim results of the STARDUST trial.

Aims & Methods: In the STARDUST study, patients with moderate-to-severe CD (CAI of 220-450) who were biologic-naïve or had prior exposure to no more than 1 biologic at baseline were treated with UST ~6mg/kg intravenously at Week 0 and single subcutaneous UST 90mg injection at Week 8. HRQoL was measured using the Inflammatory Bowel Disease Questionnaire (IBDQ). IBDQ scores were collected and the following end-points (full analysis set [FAS]) were analysed at Week 16: change from baseline in IBDQ total scores and by domain (as observed); IBDQ response, defined as increase of ≥16 points in IBDQ score from baseline; IBDQ remission defined as IBDQ score of ≥170; and IBDQ normalization as IBDQ score ≥210 (non-responder imputation).

Results: The FAS included 500 patients, of whom 292 (58.4%) were previously exposed to 1 biologic, and 208 (41.6%) were biologic-naïve. At baseline, the mean (standard deviation [SD]) IBDQ score was 127.3 (34.23) and was similar irrespective of prior exposure to biologics: 130.2 (34.91) for biologic-naïve patients and 125.2 (33.65) for patients previously exposed to 1 biologic. At Week 16, mean (SD) IBDQ total score increased to 168.8 (32.91), with a statistically significant mean change from baseline of 41.4 (33.83) (p<0.0001). Changes of total IBDQ score and by domain were all statistically significant (Table Part A). The mean (SD) change from baseline was similar regardless of prior exposure to biologics: 41.0 (33.60) for biologic-naïve patients (p<0.0001); and 41.7 (34.04) for patients previously exposed to 1 biologic (p<0.0001). More than two-thirds of patients (67.6%) achieved IBDQ response at Week 16 while 49.6% of patients achieved IBDQ remission and 6.4% achieved IBDQ normalization. Results were similar irrespective of prior exposure to biologics (Table Part B).

Conclusion: STARDUST is the first T2T trial using endoscopy to guide dose escalation in patients with CD. After 16 weeks of induction with UST, a statistically significant improvement of IBDQ score, overall and for all domains, was noted, independent of previous biologic exposure, reflecting a meaningful improvement in IBD-specific HRQoL in patients with moderate-to-severe CD.

A)	Baseline ^a : N, mean (SD)	Week 16: N, mean (SD)	Change from baseline: mean (SD), p value ^b			
Total IBDQ	465	127.3 (34.23)	462	168.8 (32.91)	41.4 (33.83)	p<0.0001
Bowel symptoms	471	41.1 (10.41)	468	53.8 (10.06)	12.7 (10.94)	p<0.0001
Emotional function	471	47.8 (14.74)	468	62.1 (14.12)	14.2 (14.00)	p<0.0001
Systemic symptoms	482	16.9 (5.77)	478	23.7 (5.98)	6.8 (6.11)	p<0.0001
Social function	476	21.3 (7.72)	472	28.8 (6.43)	7.5 (6.93)	p<0.0001

B)	Biologic-naïve at baseline: n/N, %	Had prior exposure to 1 biologic for treatment of CD at baseline: n/N, %	Total: n/N, %			
IBDQ response ^c	139/208	66.8	199/292	68.2	338/500	67.6
IBDQ remission ^d	113/208	54.3	135/292	46.2	248/500	49.6
IBDQ normalization ^e	13/208	6.3	19/292	6.5	32/500	6.4

For Section B, the non-responder imputation rule applied for missing values or early termination. ^aBaseline values for patients with at least one post-baseline assessment, as-observed data. ^bp-values based on the 2-sided Wilcoxon signed-rank test. ^cIBDQ response defined as increase in IBDQ total score of ≥16 points. ^dIBDQ remission defined as IBDQ total score ≥170. ^eIBDQ normalization defined as IBDQ score ≥210. ^f257 of 292 (88.0%) patients discontinued prior biologics due to treatment failure (inadequate response, loss of response or intolerance), of whom 116 patients (45.1%) achieved IBDQ remission, 172 (66.9%) patients achieved IBDQ response and 15 patients (5.8%) achieved IBDQ normalization. BL, baseline; CD, Crohn's disease; IBDQ, Inflammatory Bowel Disease Questionnaire; FAS, full analysis set; SD, standard deviation; UST, ustekinumab

[IBDQ at Week 16 (FAS): A) Change from BL score, overall & by domain; B) Response, remission & normalization after UST induction by line of treatment]

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P0551

INTEGRATED SAFETY ANALYSIS OF FILGOTINIB TREATMENT FOR RHEUMATOID ARTHRITIS FROM 7 CLINICAL TRIALS

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Introduction: Data from 7 clinical trials assessing filgotinib (FIL), an oral, potent, selective JAK-1 inhibitor, were integrated to assess its long-term safety in patients with rheumatoid arthritis (RA). Filgotinib provided sta-

tistically significant and clinically meaningful improvement in RA signs and symptoms, physical function, radiographic progression, and quality of life in 4 phase 3 (FINCH 1-4; NCT02889796, NCT02873936, NCT02886728, NCT03025308) and 3 phase 2 (DARWIN 1-3; NCT01668641, NCT01894516, NCT02065700) trials in patients (pts) with RA.¹⁻³

Aims & Methods: Treatment-emergent adverse events (TEAEs) from the FIL clinical program were integrated and presented for pts receiving FIL 200 mg or FIL 100 mg once daily (including pts who transitioned to FIL from placebo [PBO], methotrexate [MTX], adalimumab [ADA], or another dose of FIL) as well as pts receiving PBO, MTX, and ADA. Patients could contribute to >1 treatment group. Exposure-adjusted incidence rates (EAIRs) per 100 patient-years (PY) were calculated for adverse events (AEs) of interest per treatment. Incidence was total number of pts with events, and PY exposure was time between first and last doses. Major adverse cardiovascular events (MACE) and venous thromboembolism (VTE) were centrally adjudicated by an independent committee.

Results: Across 7 trials, 4057 pts with RA (2227 pts FIL 200 mg; 1600 pts FIL 100 mg) received >1 dose of treatment for 5493 total PY of exposure (3079.2 PY FIL 200 mg; 1465.3 PY FIL 100 mg) (Table). EAIRs of serious AEs and TEAEs leading to death in pts on FIL were, comparable to PBO, ADA, or MTX, with no dose-dependent effect (Table). EAIR for HZ were low overall, but numerically slightly higher for FIL relative to PBO, ADA, and similar to MTX. Serious infection EAIRs were comparable between pts receiving FIL 100 mg and ADA, and numerically slightly lower for FIL 200 mg and MTX. Rates of opportunistic infections (including active tuberculosis) were low overall; EAIR for FIL doses were comparable to placebo and numerically lower than ADA or MTX. Rates of MACE and VTE were numerically lower for FIL relative to PBO. Malignancies were rare overall, and rates were low in pts receiving FIL (Table). Rates of adjudicated VTE were numerically lower with both FIL doses than with MTX, ADA or PBO.

EAIR (95% CI)	FIL 200 mg (N=2227; 3079.2 PY)	FIL 100 mg (N= 1600; 1465.3 PY)	ADA (N= 325; 290.1 PY)	MTX (N= 416; 356.2 PY)	PBO (N= 781; 302.4 PY)
TE-SAEs	6.5 (5.6, 7.6)	7.7 (5.7, 10.4)	7.6 (5.0, 11.5)	7.9 (5.4, 11.4)	9.3 (5.1, 16.9)
TEAEs leading to death	0.4 (0.2, 0.7)	0.4 (0.2, 0.9)	0.3 (0.0, 2.4)	0.0	0.3 (0.0, 2.3)
Non-NMSC malignancy	0.5 (0.3, 0.8)	0.5 (0.3, 1.1)	0.7 (0.2, 2.8)	1.1 (0.4, 3.0)	1.0 (0.3, 3.1)
NMSC	0.2 (0.1, 0.5)	0.2 (0.1, 0.6)	0.0	0.3 (0.0, 2.0)	0.0
Adjudicated VTE	0.2 (0.1, 0.4)	0.1 (0.0, 0.5)	0.3 (0.0, 2.4)	0.6 (0.1, 2.2)	0.7 (0.2, 2.6)
Adjudicated MACE	0.3 (0.2, 0.7)	0.6 (0.3, 1.2)	0.3 (0.0, 2.4)	0.6 (0.1, 2.2)	1.0 (0.3, 3.1)
Serious Infections	1.7 (1.3, 2.3)	3.3 (2.2, 4.9)	3.4 (1.9, 6.4)	2.2 (1.1, 4.5)	2.3 (1.1, 4.9)
Herpes Zoster Infections	1.7 (1.3, 2.3)	1.1 (0.7, 1.8)	0.7 (0.2, 2.8)	1.1 (0.4, 3.0)	1.0 (0.3, 3.1)
Opportunistic Infections	0.1 (0.0, 0.3)	0.3 (0.1, 0.7)	0.7 (0.2, 2.8)	0.6 (0.1, 2.2)	0.0

[Total exposure to study treatments and TEAEs of Interest per 100 patient years pooled from 7 studies]

Conclusion: In this integrated analysis, FIL was well-tolerated, and no new safety concerns were identified. No clinically meaningful dose-dependent safety effects were observed. MACE and VTE were uncommon. Serious infections rates were low; HZ reactivation was infrequent. Safety results were consistent with selective JAK-1 inhibition and highlight the favourable safety and tolerability of FIL in patients with RA.

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P0552

PHASE 2A PROOF OF CONCEPT PLACEBO CONTROLLED STUDY WITH ORAL ABX464 50MG QD IN ULCERATIVE COLITIS SHOWS ENDOSCOPIC IMPROVEMENT WITH LOSS OF MICROSCOPIC DISEASE ACTIVITY IN MOST ENDOSCOPIC RESPONDERS

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Introduction: ABX464 is a first-in-class, oral, small molecule with anti-inflammatory activity. ABX464 binds the CBC complex (Cap Binding Complex), comprised of 2 proteins CBC20 and CBC80, within the cell nucleus. This leads to an increase in a single micro-RNA (miR124) expression by impacting the splicing of a single long non-coding RNA.

Aims & Methods: In the placebo controlled, centrally randomized Phase 2a Study ABX464-101, 50mg QD of ABX464 during an induction period of 8 weeks showed efficacy in moderate to severely active UC subjects who had failed or were intolerant to immunomodulators, anti-TNF α , vedolizumab, and/or corticosteroids. 32 subjects were randomized: 23 in the ABX464 group and 9 in the placebo group.

Results: The proportion of subjects achieving clinical remission (primary efficacy endpoint) was substantially higher in the ABX464 group than in the placebo group (35.0% vs. 11.1%). All endoscopic videos were centrally read. The proportions of subjects achieving endoscopic improvement (50.0% vs. 11.1%), and clinical response (70.0% vs. 33.3%) were substantially higher in the ABX464 group than in the placebo group. The difference was statistically significant for endoscopic improvement ($p = 0.0341$). Reductions in fecal calprotectin levels at week 4 and week 8 were greater in the ABX464 group than in the placebo group. Rectal biopsies were taken in 28 individuals (20 in the ABX464 group and 8 in the placebo group) at days 0 and 56, and microscopically analyzed in a blinded manner in a central laboratory. Each biopsy was scored according to 3 indices: the Geboes score, the Robarts Histopathology Index (RHI, range 0-33) and the Nancy score (NS, range 0-4). The Geboes score was transformed numerically (GBN) by assigning 1 point for each increase in subgrade (ultimate range 0-22). Of the 11 patients achieving endoscopic improvement (10 in the ABX464 group and 1 in the placebo group), all also showed histological improvement (except one with stable microscopic disease). The indices in this group dropped on average 7 points for the GBN, 15 points for the RHI and 2 points for the NI. Moreover 8/11 patients reached the microscopic

endpoint of quiescent disease (= no neutrophils, Geboes $\leq 2B.1$) Of the 17 patients who did not improve endoscopically (10 in the ABX464 group and 7 in the placebo group), 5 were also histologically non-responders and showed mean increases in the histology indices of 5, 11 and 2 points (GBN, RHI, NS resp). Leaving out one microscopically stable patient, there were still 11 of these patients who showed some degree of histologic improvement, although with smaller average drops in the indices: 4, 11 and 1 points (GBN, RHI, NS resp). The average drop was for all the indices significantly larger in the endoscopic responders than in the non-responders: GBN -6.7 versus -1.2 ($p = 0.0049$); RHI -13.3 versus -3.8 ($p = 0.0175$); and NS -1.8 versus -0.3 ($p = 0.0061$).

Conclusion: Endoscopic improvement with loss of microscopic disease activity was observed in most endoscopic responders.

Disclosure: Nothing to disclose

P0553

BI 695501 DEMONSTRATES SIMILAR EFFICACY AND COMPARABLE SAFETY TO ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH ACTIVE CROHN'S DISEASE: FINAL ANALYSIS OF THE PHASE III VOLTAIRE-CD STUDY

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Introduction: BI 695501 (adalimumab-adbm) is an approved biosimilar to adalimumab reference product (RP). This study was designed to compare the efficacy and safety of BI 695501 with EU-approved adalimumab RP in patients with moderate-to-severe active Crohn's disease.

Aims & Methods: This was a Phase III, randomised, double-blind, multicentre study (NCT02871635). Patients were anti-tumour necrosis factor-naïve, or had received infliximab but developed treatment resistance/intolerance. Patients were randomised 1:1 to receive BI 695501 or EU-approved adalimumab RP (160 mg loading dose Day 1; 80 mg Day 15; 40 mg every 2 weeks thereafter until Week 46), stratified by prior exposure to infliximab (Yes/No) and Simple Endoscopic Score for Crohn's Disease (SES-CD; $\geq 16 / < 16$). After 4 weeks, patients with clinical response to induction therapy (defined as Crohn's Disease Activity Index [CDAI] decrease ≥ 70 compared with baseline) received maintenance therapy for a further 44 weeks; at Week 24, all adalimumab RP patients switched to BI 695501. Primary endpoint was the proportion of patients with clinical response at Week 4, with an exploratory non-inferiority margin of 0.76 for the lower limit of the two-sided 90% confidence interval (CI) of the risk ratio (RR). Secondary endpoints included proportions of patients with: clinical response at Week 24, clinical remission (CDAI < 150) at Week 24, adverse events (AEs), serious AEs, and AEs of special interest. Endoscopic improvement defined by SES-CD, C-reactive protein (CRP) and fecal calprotectin were also evaluated.

Results: All 147 randomised patients were treated (BI 695501 $n=72$ /adalimumab RP $n=75$). Baseline characteristics were generally similar between treatment arms. In the full analysis set (BI 695501 $n=68$ /adalimumab RP $n=72$) at Week 4, 89.7%/94.4% of patients had clinical response (RR [90% CI] after model-based adjustment for covariates: 0.945 [0.870, 1.028]). At

Week 24, 80.9%/81.9% of BI 695501/adalimumab RP patients had clinical response, and 67.6%/75.0% had clinical remission. Safety profiles were similar between treatment arms, with no unexpected safety signals (Table). SES-CD decrease of >75% from baseline was reported for 23.5% (BI 695501) and 23.6% (adalimumab RP) of patients at Week 12, and 25.0% and 33.3% of patients at Week 48. The proportion of patients with >50 to < 90% improvement from baseline in CRP levels ranged with time from 27.9%-47.1% (BI 695501) and 26.4%-47.2% (adalimumab RP). Corresponding ranges for calprotectin improvement were 19.1%-38.2% and 25.0%-44.4%.

	BI 695501 (N=72)	Adalimumab RP ^a (N=75)
Period 1: Baseline-Week 24^b		
TEAE ^c	45 (62.5)	42 (56.0)
Drug-related TEAE	15 (20.8)	17 (22.7)
AE of special interest ^d	2 (2.8)	2 (2.7)
Period 2: Week 24-Week 46 + 10 week safety follow-up		
TEAE ^c	31 (43.1)	34 (45.3)
Drug-related TEAE	10 (13.9)	11 (14.7)
AE of special interest ^d	2 (2.8)	2 (2.7)

Data are n (%). ^aAt Week 24, all adalimumab RP patients switched to BI 695501. ^bOr within 10 weeks after the last dose of trial medication for patients who discontinued treatment before Week 24. ^cMost common TEAE categories: 'infections and infestations' (n [%]: BI 695501, 17 [23.6]; adalimumab RP, 17 [22.7]) and 'gastrointestinal disorders' (n [%]: BI 695501, 14 [19.4]; adalimumab RP, 17 [22.7]). ^dDefined as drug-induced liver injury, anaphylactic reactions, serious infection and hypersensitivity reactions. ^eMost common TEAE categories: 'infections and infestations' (n [%]: BI 695501, 14 [19.4]; adalimumab RP, 17 [22.7]) and 'gastrointestinal disorders' (n [%]: BI 695501, 6 [8.3]; adalimumab RP, 11 [14.7]). N, number of patients in analysis set; n, number of patients; TEAE, treatment-emergent adverse event.

[Summary of AEs (safety analysis set)]

Conclusion: In this controlled study, BI 695501 demonstrated similarity with adalimumab RP in patients with moderate-to-severe active Crohn's disease, in CDAI response, endoscopic improvement (SES-CD), and CRP and calprotectin levels. Exploratory analysis of CDAI response demonstrated that BI 695501 was non-inferior to adalimumab RP. Safety outcomes were similar between treatment arms. Switching from adalimumab RP to BI 695501 did not impact on clinical outcomes.

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P0554

COMPARISON OF THE EFFECTIVENESS AND SAFETY OF THE VEDOLIZUMAB THERAPY USING IN COMBINATION WITH OR WITHOUT CYCLOSPORINE IN ULCERATIVE COLITIS

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Introduction: Vedolizumab (VDZ) is indicated for the treatment of patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist. However, because of the slower onset of action of VDZ, monotherapy does not seem to be effective in more severe cases of IBD, when rapid onset of action is mandatory. Cyclosporine is an effective "rescue therapy" which may serve as a rapidly acting "bridge" to maintenance therapy with the slowly acting agents such as thiopurines in patients with severe UC. Long-term use of cyclosporine is limited because of the common occurrence of drug-related side effects. Our aim was to investigate the safety and efficacy of the combination of cyclosporine and VDZ compared to VDZ monotherapy.

Aims & Methods: In our retrospective study we analysed data of UC patients, who received VDZ therapy between January 2016 and May 2020. Patients were divided into two groups, first, who received VDZ in combination with cyclosporine induction and second, who did not take cyclosporine at the time of VDZ initiation. Therapeutic effects and safety profile were assessed from the initiation of VDZ. We compared the baseline levels of partial Mayo score, C-reactive protein (CRP), serum albumin, and hemoglobin with the values of week 14 and week 52. Moreover, we also measured the difference of these parameters between week 14 and 52.

Results: Thirty-six UC patients (42 % male) received VDZ in our institution between the study period, 13 of them concomitantly with cyclosporine (combination group). The median follow-up time was 57.4 weeks. In the combination group, 10 patients (77 %) received corticosteroid at the time of VDZ and cyclosporine induction, compared to 8 patients (35%) in the VDZ monotherapy group. There were no significant differences between the two groups in comparison of the partial Mayo score at week 0, 14 and 52, however, reduction of CRP levels was significantly higher in VDZ monotherapy group at week 14 ($p < 0.05$). Steroid could be stopped in 66% of the cyclosporine and VDZ group compared to 40% of VDZ monotherapy ($p=0.269$). After 1-year period 89% of the patients maintained receiving VDZ (100% in the cyclosporine group), and 44% still received cyclosporine. During our follow-up two patients required surgical intervention - both received VDZ monotherapy. Adverse events were observed in five cases, all of them was associated with cyclosporine use in the combination group. Side effects were mild and reversible, all of them ceased after stopping cyclosporine.

Conclusion: Our pilot study suggests that cyclosporine and VDZ can be used in combination safely with only mild side effects. This combination might reduce the need of colectomy in UC, however comparison of the effectiveness VDZ mono or combo therapy warrants further investigations with higher number of patients.

Disclosure: Nothing to disclose

P0555

ABSENCE OF BOWEL URGENCY IS ASSOCIATED WITH SIGNIFICANTLY IMPROVED INFLAMMATORY BOWEL DISEASE RELATED QUALITY OF LIFE IN A PHASE 2 TRIAL OF MIRIKIZUMAB IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Mirikizumab (miri), a humanized monoclonal antibody directed against the p19 subunit of IL-23, demonstrated efficacy and was well-tolerated in a phase 2 randomized clinical trial in patients with ulcerative colitis (UC). Bowel urgency is one of the most bothersome symptoms experienced by patients with UC and is closely tied to health-related quality of life (QoL). Here we show the relationship between patient-reported urgency and Inflammatory Bowel Disease Questionnaire (IBDQ) scores.

Aims & Methods: Patients (N=247) were randomized 1:1:1:1 to receive intravenous placebo, miri 50mg or 200mg with possibility of exposure-based dose increases, or fixed miri 600mg every 4 weeks. Patients who achieved clinical response at Week 12 (decrease in 9-point Mayo score ≥ 2 points and $\geq 35\%$ from baseline [BL], and either a decrease in rectal bleeding [RB] subscore ≥ 1 or RB subscore of 0 or 1; n=106) were re-randomized 1:1 to double-blind maintenance treatment with miri 200mg subcutaneously every 4 or 12 weeks and were treated through Week 52. Absence of urgency at Weeks 12 and 52 was defined as having no urgency for the three consecutive days prior to each scheduled visit, regardless of urgency status at BL. Patients lacking urgency data were imputed as having experienced urgency at that visit. The mean change from BL (Week 0) in IBDQ scores between patients with absence or presence of urgency at Weeks 12 and 52 was determined using analysis of covariance models.

Results: As previously reported, miri significantly reduced urgency over 52 weeks of treatment¹. In this analysis, total IBDQ score was significantly higher in patients with absence of urgency compared to those with presence of urgency at Weeks 12 and 52. [LSM (SE)]: Week 12, 179.2 (3.6) absence, 150.5 (3.2) presence, $p < 0.0001$; Week 52, 186.0 (3.91) absence, 163.1 (4.35) presence, $p < 0.0001$. A similar pattern was observed for the 4 IBDQ subscores and corresponded to percent changes from BL (% Δ BL) that were more than two times greater in patients with absence of urgency compared to patients with presence of urgency (Table).

Conclusion: In patients with absence of urgency at Weeks 12 and 52, QoL as measured by IBDQ was significantly improved compared to those with urgency. Our data demonstrate the significant negative impact of urgency on QoL in patients with UC.

References: 1P068 Mirikizumab treatment improves bowel movement urgency in patients with moderately to severely active ulcerative colitis. Dubinsky, Marla et al. Gastroenterology, Volume 158, Issue 3, S17 - S18

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	Week 12		Week 52	
	Bowel Urgency Absent N=91	Bowel Urgency Present N=156	Bowel Urgency Absent N=66	Bowel Urgency Present N=40
IBDQ total score LSM (SE)	N=90 179.2 (3.6)***	150.5 (3.2)	186.0 (3.9)***	163.1 (4.4)
% change from BL (SE) ^a	55.1 (4.3)***	22.4 (3.8)	60.4 (4.5)**	39.5 (5.0)
IBDQ Bowel Symptoms LSM (SE)	58.5 (1.1)***	47.5 (1.0)	61.2 (1.2)***	52.6 (1.4)
% change from BL (SE)	66.1 (4.4)***	28.9 (4.0)	73.9 (6.1)*	55.9 (6.8)
IBDQ Emotional Function LSM (SE)	N=90 65.0 (1.4)***	56.2 (1.3)	66.0 (1.6)*	60.2 (1.8)
% change from BL (SE)	48.3 (4.7)***	19.7 (4.2)	48.2 (4.9)*	33.5 (5.5)
IBDQ Social Function LSM (SE)	30.0 (0.7)***	24.8 (0.7)	32.1 (0.9)**	28.0 (1.0)
% change from BL (SE)	69.8 (6.8)***	23.6 (6.1)	96.3 (10.7)*	49.7 (12.0)
IBDQ Systemic Symptoms LSM (SE)	25.6 (0.6)***	21.8 (0.5)	26.5 (0.7)***	22.6 (0.8)
% change from BL (SE)	56.1 (4.9)***	27.1 (4.4)	63.5 (5.4)***	33.0 (6.0)

LSM = least squares mean; SE = standard error; BL = baseline (Week 0); IBDQ = Inflammatory Bowel Disease Questionnaire; ^aPercent difference of LS Mean = (LS Mean Change from baseline*100)/(Observed Mean at week 12/52 - Observed Change Mean at week 12/52) for each group; * $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$ vs bowel urgency = yes

[Table. IBDQ Scores in UC Patients with Absence or Presence of Urgency]

P0556

LONG TERM USE OF BIOLOGIC AND IMMUNOMODULATORS IN INFLAMMATORY BOWEL DISEASE (IBD) AND THE RISK OF DEVELOPING CANCER: A RETROSPECTIVE REVIEW FROM A GENERAL HOSPITAL IN UNITED KINGDOM

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Introduction: Cancer is along term complication in a patient with Inflammatory bowel disease (IBD). Anti-TNF and immunomodulators (Azathioprine and Methotrexate) have been widely used in the treatment of IBD. These might contribute to increase the risk of cancer despite the control of an underlying diseases.

However available data is inconsistent, despite the fact that It has been more than 2 decades since infliximab; the first tumor necrosis factor- α (TNF) inhibitor, received its initial marketing approval from the US Food and Drug Administration for the treatment of Crohn's disease. (1)

Safety issues are a major concern for patients considering treatments for inflammatory bowel disease (IBD) , specifically worries related to risk of malignancy.

Aims & Methods: In our study we performed an observational analysis to determine whether Anti TNF biologics -Infliximab (Remicade) or adalimumab (Humira) or biosimilar - long term usage is associated with malignancy in IBD adults patients. A retrospective, observational, cohort study of patients with inflammatory bowel disease treated with Anti-TNF as first-line anti-tumour necrosis factor treatment at a general hospital.

Inclusion criteria are: Patient above 18 who received/receiving Anti-TNF (with or without immunomodulators) for at least 3 years.

Data was extracted from the related infusion clinic and pharmacy database .Patients included in the study were under our hospital care for their IBD at our IBD clinics, or being admitted at our hospital. We reviewed each patient's case records (paper-form and electronic on the hospital's database) , with all related investigations including radiological tests.

Results: Total 105 cases were reviewed and 70 cases met the inclusion criteria. Male 61% (n=43) and female 39% (n=27). Crohn's disease 73% (n = 51) and Ulcerative colitis 27%. (n = 19) The mean disease years was 14 $\pm$ SD 3.6 years . Range of usage of Anti-TNF was (3-15years), while the mean usage duration was 6.9 $\pm$ SD 3.6 years . Out of these patients 5 cases of malignancy were found; (4 male and 1 female).

Analysis revealed that only 5 cases of malignancy were found; (4 male and 1 female). All males were ulcerative colitis and female had Crohn's disease. Mean age of cancer patient was 67.4 $\pm$ SD 9 years.

With further analysis pertaining to each type of cancer in relation to the IBD , there was no significance between risk of cancer development and Anti-TNF therapy as solo therapy (P value 0.36).

Conclusion: Our study supports that long term use of monotherapy with an anti-TNF is safe in IBD patients. Although there is a risk associated with combination treatment of ant-TNF with immunomodulators, however our study also revealed that there is risk of developing cancers but these developed after a decade of combination treatment.

Strength of our study is the long period of observation extending to 15 years. Weakness of the study which could be utilized in future analysis is the inclusion of smoking history, BMIs, disease severity and complexity, related to IBD condition.

This analysis provides a useful perspective about infliximab and combination treatment safety from the cancer perspective, nevertheless further research is warranted to expand the current evidence and long term safety profile.

References: 1 Remicade® (infliximab): 20 years of contributions to science and medicine Richard Melsheimer, Anja Geldhof, Isabel Apaolaza, Thomas Schaible Biologics.; 2019 Jul 30. doi: 10.2147/BTT.S207246 2 Association Between Tumor Necrosis Factor- α Antagonists and Risk of Cancer in Patients With Inflammatory Bowel Disease .Nynne Nyboe Andersen, JAMA. 2014;311(23):2406-2413. doi:10.1001 3 SYSTEMATIC REVIEWS AND META-ANALYSES .Fasiha Kanwal, Section Editor Biologic Therapies and Risk of Infection and Malignancy in Patients With Inflammatory Bowel Disease: A Systematic Review and Network Meta-analysis Stefanos Bonovas, Clinical Gastroenterology and Hepatology 2016;14:1385-1397 4 Drug Therapies and the Risk of Malignancy in Crohn's Disease: Results From the TREAT™ Registry Gary Lichtenstein; American Journal of Gastroenterology. 109(2):212-223, FEBRUARY 2014 5 Peyrin-Biroulet L, Khosrotehrani K, Carrat F, et al. Increased risk for nonmelanoma skin cancers in patients who receive thiopurines for inflammatory bowel disease. Gastroenterology. 2011;141:1621-1628 6 Long MD, Martin CF, Pipkin CA, et al. Risk of melanoma and non-melanoma skin cancer among patients with inflammatory bowel disease. Gastroenterology. 2012;143:390-399.e1. 7 Abbas et al. Risk of melanoma and non-melanoma skin cancer in ulcerative colitis patients treated with thiopurines: a nationwide retrospective cohort. Am J Gastroenterol. 2014;109:1781-1793 8 British association of dermatologist . <http://www.bad.org.uk/for-the-public/patient-information-leaflets/azathioprine#>

Disclosure: Nothing to disclose

P0557

FREQUENCY AND EFFECTIVENESS OF EMPIRICAL ANTI-TNF DOSE INTENSIFICATION IN INFLAMMATORY BOWEL DISEASE: SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Loss of response to anti-TNF (tumor necrosis factor) therapies in inflammatory bowel disease occurs in a high proportion of patients. However, the precise incidence of dose intensification (DI) and its effectiveness remain unclear.

Our aims were:

- 1) To evaluate the need of DI of anti-TNF therapy either by increasing the dose or decreasing doses' interval;
- 2) To evaluate possible variables influencing its requirement;
- 3) To assess the effectiveness of empirical DI.

Aims & Methods: Bibliographical searches were performed in Pubmed, Embase, Cochrane Library and CINAHL. Selection: prospective and retrospective studies assessing the loss of response to anti-TNF therapy, considered as the need of DI, in Crohn's disease (CD) and ulcerative colitis (UC) patients treated for at least 12 weeks with an anti-TNF drug [infliximab (IFX), adalimumab (ADA), certolizumab pegol or golimumab]. Exclusion criteria: Studies using anti-TNF as prophylaxis for postoperative recurrence in CD or those where DI was based on therapeutic drug monitoring.

Meta-analysis was conducted and data were stratified by medical baseline condition (UC vs. CD), anti-TNF drug and follow-up. Effectiveness was assessed by intention-to-treat. Subgroup analyses were performed to explore heterogeneity.

Results: 148 studies (26,886 patients) were included. The overall rate of DI requirement after 12 months follow-up was 32% (95% confidence interval (CI): 27-37%, $I^2=96\%$, 42 studies) for naïve patients and 37% (95%CI: 24-51%, $I^2=91\%$, 11 studies) for non-naïve patients, with no statistical differences between subgroups. Rate of DI requirement for naïve patients after

36 months follow-up was 37% (95%CI: 29-45%, $I^2=96\%$, 20 studies). Rate of DI requirement after 12 months follow-up was statistically higher in UC than in CD patients ($\chi^2=13$; $p=0.0003$; $I^2=92\%$), either treated with IFX ($\chi^2=8.9$; $p=0.003$; $I^2=89\%$) or ADA ($\chi^2=9$; $p=0.002$; $I^2=89\%$).

The overall short-term response rates to empirical DI were 69% (95%CI: 64-75%; $I^2=75\%$; 30 studies) and 65% (95%CI: 43-87%; $I^2=82\%$; 5 studies), in naïve and non-naïve patients, respectively. The overall remission rates to empirical DI were 49% (95%CI: 39-58%; $I^2=89\%$; 23 studies) and 30% (95%CI: 12-48%; $I^2=86\%$; 6 studies) in naïve and non-naïve patients. No significant differences between naïve and non-naïve patients were reported either in response or remission rates.

DI requirement in naïve patients after 12 months follow-up, plus short-term response and remission rates to DI by anti-TNF agent and medical condition are summarised in table 1.

Anti-TNF	UC/CD	DI requirement (% 95% CI)	I^2 (%)	Number of studies included	Response rate (% 95%CI)	Number of studies included	Remission rate (% 95%CI)	Number of studies included
IFX	UC+CD	35 (26-43)	97	39	71 (66-75)	26	51 (40-63)	15
IFX	UC	47 (35-59)	95	10	78 (66-91)	6	57 (35-78)	8
IFX	CD	25 (16-33)	96	17	69 (65-74)	17	45 (34-57)	6
ADA	UC+CD	23 (16-31)	93	12	62 (54-69)	4	39 (26-52)	8
ADA	UC	31 (24-37)	85	6	58 (48-68)	1	17 (7-27)	1
ADA	CD	15 (7-23)	77	6	68 (55-81)	3	45 (30-59)	6

[Table 1: Dose intensification requirement, response and remission rates by subgroup analysis]

Conclusion: Loss of response to anti-TNF agents —and consequent DI— occurs frequently in both UC and CD, with an overall rate of DI requirement of 32% at one year and 37% at 3 years for naïve patients. Empirical DI is a relatively effective therapeutic option with response and remission rates after DI of 69% and 49%, respectively.

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P0558

TRANSLATIONAL BIOMARKERS FOR SELECTIVE, ORAL, SMALL MOLECULE $\alpha_4\beta_7$ INHIBITOR MORF-057

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Introduction: Inhibition of $\alpha_4\beta_7$ is a clinically validated mechanism for the effective treatment of inflammatory bowel disease (IBD) and MORF-057 is an orally bioavailable small molecule inhibitor of $\alpha_4\beta_7$. Nonclinical pharmacology studies of MORF-057 have demonstrated potent and selective inhibition of $\alpha_4\beta_7$ in biochemical and cell based assays, inhibition of gut homing of inflammatory cells in mice, and an increase in $\alpha_4\beta_7$ central memory T cells in monkeys (Wong et al. DDW, 2020). The current studies establish translational biomarker assays *ex vivo* in human whole blood and *in vivo* in animals to support the clinical development of MORF-057.

Aims & Methods: Receptor occupancy assays for $\alpha_4\beta_7$ and $\alpha_4\beta_1$ were established under physiologic conditions including natural ligands and metal, specifically excluding the addition of manganese that affects inhibitor binding. A novel multimeric Mucosal Vascular Addressin Cell Adhesion Molecule 1 (MAdCAM-1) ligand was used to increase avidity for $\alpha_4\beta_7$ in human whole blood without the need for manganese used in previously reported assays. The receptor occupancy assay for $\alpha_4\beta_1$ used a Leucine-Aspartic Acid-Valine (LDV) peptide. Using these assays, MORF-057 was assessed for its 50% and 90% inhibition constants (IC_{50} and IC_{90}) in fresh human blood from healthy donors. Cynomolgus monkey and human blood was also characterized for the presence of $\alpha_4\beta_7$ high B cells, effector and central memory T cells, and the expression of CCR9 mRNA. In addition to blood-based biomarkers, intestinal tissue can also be assessed during clinical trials in patients. To explore effects on cellular dynamics in tissue, naïve mice were treated with a close analogue of MORF-057 and trafficking of $\alpha_4\beta_7$ positive lymphocytes to Peyer's Patches was assessed.

Results: MORF-057 was found to be a highly potent and selective inhibitor of $\alpha_4\beta_7$ in human whole blood achieving IC_{90} at 20.1 nM and being >600-fold selective against $\alpha_4\beta_1$ (Table). Low levels of $\alpha_4\beta_7$ high T and B cells, and CCR9 transcript were observed in blood. Inhibition of $\alpha_4\beta_7$ resulted in decreased cellularity as early as 48 hours. Peyer's patches decreased by more than two-thirds and the reduction was sustained with prolonged inhibitor dosing.

Conclusion: Consistent with results in cell lines, MORF-057 is a potent and selective inhibitor of $\alpha_4\beta_7$ in human whole blood using a receptor occupancy assay conducted under physiologically relevant conditions. Human blood contained low, but detectable, levels of cell populations reported to be sensitive to $\alpha_4\beta_7$. Inhibition of $\alpha_4\beta_7$ in mice resulted in decreased cellularity in Peyer's patches, secondary lymphoid structures responsible for immunoglobulin production and important to the pathophysiology of IBD. Importantly, the reported assays can be applied to investigate the pharmacology of MORF-057 in clinical studies.

	IC_{50} (nM)	IC_{90} (nM)
$\alpha_4\beta_7$	3.54 ± 0.63	20.1 ± 6.0
$\alpha_4\beta_1$	$2,160 \pm 710$	$14,100 \pm 6,700$
Selectivity	610	700

[MORF-057 is a potent and selective inhibitor of $\alpha_4\beta_7$ over $\alpha_4\beta_1$ in human whole blood *ex vivo*. Values are the mean $\pm$ standard deviation of 6 donors.]

References: PRECLINICAL CHARACTERIZATION OF AN ORAL SMALL MOLECULE INHIBITOR TARGETING THE INTEGRIN $\alpha_4\beta_7$ FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASES (IBD). Jamie Wong et al. Digestive Disease Week ePoster Tu1283

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P0559

EFFECT OF 52 WEEKS OF MIRIKIZUMAB ON INFLAMMATORY BOWEL DISEASE QUESTIONNAIRE SCORES IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE

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Introduction: Mirikizumab (miri; IL-23p19 antibody) is a humanized, IgG4 monoclonal antibody specifically targeting the p19 subunit of IL23. Miri has demonstrated clinical efficacy in Phase 2 trials in psoriasis and ulcerative colitis and resulted in significant improvements in health-related quality of life (HRQoL) as measured by the inflammatory bowel disease questionnaire (IBDQ) after 12 weeks of induction treatment in a Phase 2 trial (SERENTIY; NCT02891226) in patients with moderate-to-severely active Crohn's disease (CD). The Week 52 IBDQ results are reported here.

Aims & Methods: Maintenance period aims were to evaluate the long-term efficacy and safety of miri administered over one year. Patients with moderate-to-severe CD were randomized 2:1:1:2 across 4 treatment arms (PBO, 200, 600, 1000mg miri, administered intravenously (IV) at Weeks 0, 4, 8). Patients who received miri and achieved ≥ 1 point improvement at Week 12 in Simple Endoscopic Score for Crohn's Disease (SES-CD) were re-randomized 1:1 into double-blind maintenance to continue IV treatment assignment (IV-C; N=41) or to 300mg miri SC (SC; N=46). IBDQ score change from baseline (induction phase), IBDQ response, and IBDQ remission were assessed through Week 52. Group comparisons for IBDQ score change from baseline were done using an ANCOVA model with IBDQ score baseline and response status as covariates.

Results: Baseline demographics and disease characteristics as well as Week 52 IBDQ outcomes are provided (Table 1). Among the Week 12 miri induction endoscopic improvers, IBDQ response rates at Week 52 were 75.6% (31/41) and 80.4% (37/46) and IBDQ remission rates were 65.9% (27/41) and 67.4% (31/46) in the IV-C and SC groups, respectively. The change from baseline in IBDQ was similar in both groups, with a total change of 64.3 and 66.4 points in the IV-C and SC groups, respectively. Changes from baseline in IBDQ at Week 52 were significantly higher for patients who achieved PRO response (decrease in SF or AP ≥30% and no worse than baseline) and PRO remission (SF ≤2.5 and AP ≤1 and no worse than baseline) at Week 52 (64.0 and 70.3) versus those who did not achieve these endpoints (37.8 and 45.6; p< 0.001 in both cases).

Conclusion: These data affirm the sustained efficacy of miri in producing meaningful improvements in HRQoL as measured by the IBDQ through 52 weeks of treatment.

Week 0 (Baseline)		Week 52			
Mean ± (SD) unless otherwise noted	miri IV N=41	miri SC N=46		miri IV N=41	miri SC N=46
Weight, kg	72.8 (15.0)	75.1 (18.4)	Total IBDQ score	188.5 (26.6)	180.8 (25.4)
Age, years	40.0 (13.2)	37.8 (11.9)	IBDQ response ^a , n (%)	31 (75.6)	37 (80.4)
Gender, male (n, %)	21 (51.2)	23 (50.0)	IBDQ remission ^b , n (%)	27 (65.9)	31 (67.4)
Concomitant CD Medications (n, %)					
Corticosteroids	8 (19.5)	11 (23.9)	IBDQ score ΔBL ^c	64.3	66.4
Azathioprine	0	1 (2.2)			
Methotrexate	0	0			
Previous Biologic Exposure (n, %)	25 (61.0)	27 (58.7)			
IBDQ	126.2 (30.8)	113.4 (37.7)			
CRP (median, Q1-Q3)	6.0 (2.1-20.6)	6.3 (2.4-12.9)			

^aIBDQ response: ≥16-point improvement in IBDQ score; ^bIBDQ remission: total IBDQ score ≥170; ^c ΔBL: as observed; change from baseline; ^d Endoscopic improvement: ≥1 point improvement in SES-CD at Week 12.

[Week 52 IBDQ Scores in Week 12 Endoscopic Improvers^d]

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P0560

COMPARATIVE EVALUATION OF TREATMENT PERSISTENCE AND DOSE INTENSIFICATION IN PATIENTS WITH CROHN'S DISEASE TREATED WITH USTEKINUMAB VERSUS VEDOLIZUMAB

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Introduction: Ustekinumab (UST) and vedolizumab (VDZ) are approved biologic therapies for moderate-to-severe Crohn's disease (CD). A previous US real-world study revealed a monthly healthcare cost that was significantly higher in patients receiving UST compared with VDZ.

Aims & Methods: This retrospective cohort study aims to compare treatment persistence and dose intensification as indicators of real-world effectiveness in patients with CD receiving UST or VDZ. The IBM Truven Health MarketScan database was used to identify adult patients initiated on UST or VDZ (index drug) on or after September 26, 2016, who had CD as the latest relevant diagnosis on or before index drug initiation (index date), had ≥6 months of data available both before and after the index date, completed induction, and initiated maintenance therapy. The follow-up period spanned from the index date up to the end of data availability. Entropy balancing was used to address confounding factors. Treatment persistence and dose intensification were evaluated overall and in the subgroup of biologic-naïve patients, defined as those with no pre-index biologic therapy. Treatment persistence was defined as time from the index date to either treatment discontinuation (event) or end of follow-up (censor). A sensitivity analysis evaluated treatment persistence starting from the maintenance phase initiation. Dose intensification was identified as 2 consecutive shortened dosing intervals (defined as time between 2 consecutive doses ≤49 days), or 1 shortened dosing interval followed by treatment discontinuation. For UST, an intravenous injection during the maintenance phase also indicated a dose intensification. Treatment persistence and time to dose intensification rates were assessed at predefined time points using weighted Kaplan-Meier analyses and compared between UST and VDZ patients using log-rank tests.

Results: The 599 (117 biologic-naïve) UST- and 589 (172 biologic-naïve) VDZ-treated CD patients who met eligibility criteria had similar baseline characteristics. Disease location, follow-up duration, and prior therapies and surgeries were also comparable. Characteristics were similar in biologic-naïve patients. Treatment persistence rates assessed from the index date were similar in UST and VDZ patients, with no statistically significant differences at all key time points (UST=82.1%, VDZ=76.5%; $P=0.17$, at 12 months).

In contrast, treatment persistence rates assessed from the maintenance phase initiation were slightly higher in UST vs VDZ patients at all predefined time points (UST=77.8%, VDZ=72.8%; $P=0.02$, at 12 months). In biologic-

naïve patients, treatment persistence rates at all key time points were not statistically significantly different in UST and VDZ patients when assessed from the index date (UST=87.0%, VDZ=78.6%; $P=0.44$, at 12 months) or from the maintenance phase initiation (UST=86.3%, VDZ=74.9%; $P=0.18$, at 12 months). Overall, dose intensification rates were similar in UST and VDZ patients at all key time points (UST=32.7%, VDZ=29.3%; $P=0.97$, at 12 months), with a higher difference in biologic-naïve patients (UST=32.3%, VDZ=21.5%; $P=0.43$, at 12 months).

Conclusion: In a real-world cohort of patients with CD, although substantially higher healthcare costs were previously shown to be associated with UST versus VDZ, treatment persistence and dose intensification were similar in patients treated with UST and VDZ. Comparative analyses to assess other clinical outcomes for these medications are warranted.

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P0561

PRE-BIOLOGIC SCREENING IN A HIGH-RISK AREA: ARE WE ADHERING TO GUIDELINES?

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Introduction: Newham University Hospital, Barts Health NHS Trust, serves the London Borough of Newham which had the highest incidence of tuberculosis in the UK at 78.0 per 100,000 in 2014. Newham also has the highest average annual rate of new reported acute hepatitis B infection in the UK. There have been clear guidelines on pre-biologic screening for opportunistic infections since 2014. Our aim is to assess whether patients who are on biologic therapy have been appropriately screened prior to initiation of biologic therapy.

Aims & Methods: To assess whether patients who are on biologic therapy have been appropriately screened prior to initiation of biologic therapy. A retrospective review of all inflammatory bowel disease (IBD) patients on the biologic database was performed in November 2019. Patients who were initiated on biologics prior to the publication of guidelines in June 2014 were excluded.

We evaluated whether there was evidence of the following laboratory and radiographic tests prior to the initiation of biologic therapy; hepatitis B Surface Antigen (HbsAg), hepatitis B Core Antibody (HbcAb), hepatitis C IgG, HIV I+II antibody, EBV IgG, VZV IgG, Interferon-gamma release assay (IGRA) and chest X-ray.

Results: The total number of patients was 63. 31 patients (49.2%) had latent tuberculosis testing with Interferon-gamma release assay (IGRA) testing and two were positive. Screening with chest X-ray was better with 58.9% concordance. 36 patients had normal CXRs and one had an appearance of a granuloma.

In comparison, viral screening had higher completion rates. Hepatitis B Surface Antigen (HbsAg) was sent in 53 patients (84%) and all were negative. Hepatitis B Core Antibody (HbcAb) was sent in 23 patients (36.5%) and one was positive. One patient was HbcAb positive but HbsAg negative. In terms of Hepatitis C, 51 patients (80.9%) had Hepatitis C IgG sent and all were negative. All 50 patients (79.3%) who were tested for Human immu-

nodeficiency virus (HIV I+II antibody) were negative. Epstein Bar Virus IgG was sent in 20 patients (31.7%), out of which, 15 were negative. Varicella-Zoster Virus IgG was sent in 39 patients (61.9%) and two were positive. An infection history was not taken, for either bacterial, fungal or viral infections and Bacille Calmette-Guerin (BCG) vaccination status was not documented. No documentation was present regarding measles status. Routine vaccination status was not confirmed for diphtheria, poliomyelitis, pertussis, tetanus or Human Papilloma Virus (HPV). Prior to initiation of immunomodulation, vaccination was not considered for pneumococcal or influenza infections.

Conclusion: Despite suboptimal pre-biologics screening in this high-risk region of East London for Tuberculosis and Hepatitis B, no cases of reactivation of either Tuberculosis or Hepatitis B have been identified to date. The results suggest that clinicians are requesting some tests but not all. Following on from these results, we will be streamlining the process for ensuring all tests are performed prior to biologic initiation with a checklist proforma for the patients notes and on our biologics database for all prescribing gastroenterologists, as per European Crohn's and Colitis Organisation (ECCO) guidelines.

Disclosure: Nothing to disclose

P0562

GB004 EXHIBITS PROTECTIVE EFFECTS DIRECTLY ON EPITHELIAL CELLS USING EX VIVO ORGANOID AND MONOLAYER CULTURES

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Introduction: GB004 is a small molecule stabilizer of hypoxia inducible factor (HIF-1α), a key transcription factor involved in the protective cellular responses at the intersection of hypoxia and inflammation. GB004 has demonstrated efficacy in mouse models of colitis, induces HIF-1α target genes and improves barrier integrity and reduces barrier permeability.

Aims & Methods: To further explore direct effects of GB004 and translatability to human gastrointestinal epithelial cells, mouse and human organoid and 2D monolayer cultures were assessed for induction of HIF-1α target genes, formation of tight junctions and improvement in barrier integrity. Mouse organoids were derived from the small intestine of C57BL/6 mice and cultured in IntestiCult Organoid Growth Media (Stem-Cell Technologies, Cambridge, MA). Organoids were pretreated for 1 hour with GB004 followed by stimulation with IFNγ to activate the organoids. RNA was isolated from the organoids and gene expression analysis was performed. Human Repligut assays were performed at Altis Biosystems (Chapel Hill, NC) by proliferating and differentiating human-derived intestinal epithelial cells on a 2D monolayer platform. These monolayers were assessed with GB004 treatment under normal healthy conditions or with cytokine stimulated conditions (TNFα or IFNγ) to induce barrier damage. Barrier integrity was assessed through measuring Transepithelial Endothelial Electric Resistance (TEER). HIF-1α target genes were assessed in cell lysates and tight junction formation and adhesion molecules were investigated by immunofluorescence staining.

Results: Similar to observations in mouse models of colitis, GB004 treatment of mouse intestinal organoids induces HIF-1α dependent genes including protective barrier genes, junctional proteins, and anti-apoptotic genes. In healthy, human intestinal-derived monolayer cultures, GB004 also induces HIF-1α dependent genes and maintains barrier integrity. To induce barrier disruption, human differentiated monolayers were treated with cytokines which resulted in cellular apoptosis and loss of barrier integrity. GB004 treatment of these damaged monolayers results in reduced

cell death and improved barrier integrity. Immunofluorescence staining with tight junction protein (ZO-1) and adhesion molecule (claudin 1) shows improved staining and junction formation with GB004 treatment.

Conclusion: GB004 demonstrates direct protective effects on mouse and human-derived organoid and 2D monolayer epithelial cultures in vitro by reducing cell apoptosis, preserving tight junctions, and improving barrier integrity. Data generated in human intestinal-derived monolayers support direct barrier integrity effects similar to data generated in mouse organoid assays and efficacy studies in mouse colitis. A clinical study of GB004 has recently completed enrollment in patients with ulcerative colitis (NCT03860896). Sponsored by GB004, Inc., a wholly owned subsidiary of Gossamer Bio, Inc.

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P0563

INTRAVENOUS USTEKINUMAB REINDUCTION IS EFFECTIVE IN PRIOR BIOLOGIC REFRACTORY PATIENTS WITH CROHN'S DISEASE ALREADY ON 4 WEEKLY DOSING: A REAL-WORLD CASE SERIES

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Introduction: Ustekinumab (UST) targets the common subunit (p40) of interleukins 12 and 23.(1) It is approved for intravenous (IV) induction of remission in moderate-to-severe Crohn's Disease (CD), followed by subcutaneous (SC) doses for maintenance of remission.(2, 3) The role of IV reinduction of UST in patients (pts) already on every 4-week (Q4) maintenance with partial or loss of response (LOR) is unclear (4).

Aims & Methods: Assess response and remission rates for UST IV reinduction in pts with CD with partial or LOR who are already on Q4 SC dosing. Retrospective cohort study in a tertiary care Canadian IBD center. We assessed clinical, endoscopy/imaging, and biochemical response/remission according to clinical PGA(5, 6), Harvey-Bradshaw Index (HBI), mucosal healing parameters, and C-reactive protein (CRP) values, respectively, as well as the safety parameters.

Results: Fifteen pts, median age 52 years (33 - 66 years), 66.7% female (10/15), with 12/15 (80%) bio-exposed, and 40% failed 2 prior biologics (Table 1) underwent IV reinduction with 90 mg/kg UST between May 2018 to February 2020. Reasons for reinduction were: PGA active disease (15/15, 100%), HBI >7 (9/15, 60%), endoscopy/imaging active disease (ulcers, active inflammation) (15/15, 100%), and CRP > 5 mg/dl (5/15, 33.3%). Mean time to IV reinduction since UST was started was 60.1 weeks (w) (19-138 w). Mean time to assessment after reinduction was 14.9 w (4-29 w) for PGA/ HBI scores, 30.9 w (4-58 w) for endoscopy/imaging, and 28.4 w (5-50 w) for CRP. According to PGA, after reinduction 10/15 pts (66.7%) had clinical response (>50% improvement in symptoms) with 8/15 pts (53.3%) achieving clinical remission. According to HBI, 11/14 (78.6%) achieved clinical response (HBI reduction > 3 points) and 8/14 pts (57.1%) were in remission (HBI < 4 points) after reinduction. Based on a paired t-test, the HBI showed a statistically significant mean decrease of 2.4 points after reinduction (95%CI: -3.8 - -0.9; p=0.0034). Eleven pts had paired CRP values before and after reinduction, mean value of 10.1 mg/dL (0.6 - 43.1 mg/dL) and 8.1 mg/dL (0.6 - 31.1 mg/dL), respectively. Based on a paired t-test, the mean CRP dropped on average by 2.1 mg/dL (95% CI: -5.8 - 1.6 mg/dL; p=0.24). Eight pts had paired endoscopy/imaging before and after rein-

duction, with 7/8 pts (87.5%) achieving response (improvement from previous study), and 5/8 pts (62.5%) achieving remission (absence of endoscopic ulcers or imaging inflammation). No severe adverse reactions were seen, and 1/15 pts (6.7%) developed headache, not associated with UST.

Conclusion: In a prior biologic refractory CD population who had already been escalated to SC Q4 dosing, UST IV reinduction was safe and recaptured clinical response and remission in over 50% of subjects through a range of clinical and objective measurements. This strategy should be routinely considered before switching out of class.

Patients characteristics (N=15)	n (%)
Females, n (%)	10 (66.7)
Median age - years (range)	52 (33-66)
Mean disease duration - years (range)	18,13 (0 - 40)
Disease Location, n (%)*	Colonic / Ileocolonic 2(13.3) / 11 (73.3)
	Upper gastrointestinal tract / Perianal 2 (13.3) / 3 (20)
Previous surgery, n (%)	None 7 (46.7)
	Colectomy / Ileocolonic resection 2 (13.3) / 5 (33.3)
	Small bowel resection 1 (6.7)
Previous therapies, n (%)	Immunosuppressants / Steroids 7 (46.7) / 11 (73.3)
Biologics (previous to UST), n (%)	Bio-naïve 3 (20)
	Infliximab/Adalimumab 9 (60) / 7 (46.7)
	Vedolizumab 2 (13.3)
N of previous biologics, n (%)	One biologic / Two biologics 6 (40) / 6 (40)

[Table 1. *Some patients had more than one disease location]

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COGNITIVE BEHAVIORAL MINDFULNESS INTERVENTION WITH QUOTIDIAN HOME PRACTICE FOR CROHN'S DISEASE PATIENTS: EFFECT ON PHYSICAL AND MENTAL FUNCTIONING, AND DISEASE-COPING STRATEGIES

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Introduction: Crohn's Disease (CD) patients suffer chronically from physical symptoms and psychological distress, and have poor disease-coping strategies (Sarid, 2017). We reported that a Cognitive Behavioral Mindfulness Intervention (CBMI) program improves mental health in CD patients with mild and moderate disease severity, and increases their quality of life (Sergienko, 2020). Yet, it is unknown whether daily exercising of CBMI associates with the degree of improvement. We aim to assess whether at least once-a-day exercise of CBMI techniques boosts the symptomatic and psychological betterment. A second aim is to determine the benefit on patients' disease-coping strategies.

Aims & Methods: Consecutively recruited adult (>18 years) patients with active CD (n=99) attending an out-patient clinic at a tertiary hospital were taught CBMI techniques weekly over a 3 month period by specially trained social workers, using Skype™. Patients were asked to exercise these techniques for minimum 10 minutes, at least once-a-day, and to report their adherence to this protocol by a smartphone app daily. Clinical (by a physician) and psychological (self-report) questionnaires were completed at baseline (T1) and after 3 months of CBMI (T2). Disease activity was assessed by the Harvey-Bradshaw Index (HBI). Quality of life was assessed by Short-Form 12 (SF-12) that measures physical and mental health. Psychological distress was assessed by the Brief Symptom Inventory that includes the mental health variables of depression, anxiety and somatization. Personal coping resources were assessed by the Brief COPE questionnaire of emotion-focused and problem-focused coping. Social support was assessed by the Multidimensional Scale of Perceived Social Support. Fatigue was assessed by the FACIT scale. CBMI exercise rates were calculated from patients' daily reports over the 3 month period (T1 to T2). Statistics included Mann-Whitney, Kruskal-Wallis, Chi-Square and Spearman's rho.

Results: Patients (n=99) had a mean age of 33.7 (SD 11.4) years, and a mean disease duration of 9.15 (SD 8.5) years; 64.6% were female, 87% non-smokers, 79% with higher education, and 76% working. In the 3 month period, 97 (98%) patients reported exercising at least once-a-day on all days, with 50% of patients exercising twice-daily on 64% of the days. Disease severity in the cohort (HBI score 5-16) correlated negatively with once-a-day exercising ($r=-.258$, $p=.010$). In patients with mild disease at T1 (HBI 5-7), the exercise rate correlated negatively with depression ($r=-.367$, $p=.024$), anxiety ($r=-.350$, $p=.031$) and somatization ($r=-.361$, $p=.026$), and correlated positively with physical health ($r=.475$, $p=.003$), emotion-focused coping ($r=.479$, $p=.002$), problem-focused coping ($r=.413$, $p=.010$) and perceived family support ($r=.326$, $p=.045$). In patients with moderate disease at T1 (HBI 8-16), exercise correlated negatively with anxiety ($r=-.336$, $p=.018$), somatization ($r=-.341$, $p=.016$) and fatigue ($r=-.307$, $p=.032$), and correlated positively with emotion-focused coping ($r=.328$, $p=.021$). Demographic parameters had no significant correlations with any of the measures.

Conclusion: Exercising CBMI daily for at least 10 minutes was associated with better physical health, lessened anxiety, depression and somatic symptoms, and more efficient coping strategies. The response was better in patients with mild disease. These findings may indicate an important role of daily exercise. The data support the integration of CBMI practiced daily into the life of CD patients.

References: Sergienko R, Goren G, Sarid O et al. DDW 2020: Tu1847. Sarid O, Slonim-Nevo V, Pereg A et al. PLoS One. 2017 Feb 28;12(2):e0172779. doi: 10.1371/journal.pone.0172779.

Disclosure: Nothing to disclose

P0565

IMMUNOSENESCENCE IS A FACTOR IN RESPONSE TO INFLIXIMAB THERAPY IN IBD PATIENTS OVER 65 YEARS OF AGE

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Introduction: Age related immunosenescence affects the quantity and quality of T and B cell immune responses with a progressive reduction in the ability to trigger effective antibody responses to newly encountered antigens. Secondary loss of response to biologics is associated with antibody formation and resultant lower drug trough levels, while higher trough levels could increase infection risk. The impact of immunosenescence on response to Infliximab therapy is unclear.

Aims & Methods: A retrospective nested case-control study of maintenance phase Infliximab trough and antidrug antibody (ADA) levels in elderly >60 years, as defined by the European Crohn's and Colitis Organisation and younger IBD patients was undertaken. Low and suboptimal troughs were defined as < 1 ug/ml and < 5ug/ml respectively. Patients on increased treatment schedules / doses were excluded, as were patients with an elevated CRP, indicative of a flare. Continuous data and categorical data were compared using a Student t test and a Chi² test respectively, p< 0.05 was considered significant.

Results: 161 subjects on maintenance infliximab were included, n=26 (16%) >60 years, (range 60- 84), 84 (52%) males, 94 (68%) with Crohn's disease. Demographics were similar among groups. Overall 25 (15%) had a low trough and 86 (53%) suboptimal trough levels. Of these 4 (2%) with a low trough and 9 (6%) with a suboptimal result were excluded due to an elevated CRP. There was no statistically significant difference in mean trough levels (6.4 v 5.7 mg/ml) or proportion of low (n=2 (9%) v n=19 (14%) and suboptimal troughs (n=9 (39%) v 68 (51%) based on age > or < 60 years. However when we analysed the data based on age >65 years, younger patients were more likely to have a suboptimal trough 3/14 (21%) versus 74/138 (54%) OR 4. p< 0.04, 95%CI 1.1- 14.9. Although the frequency of a low trough remained similar 18/143 (13%) v 2/14 (14%). ADA levels were available in 9 (34%) older and 98 (67%) of younger subjects. While there was a trend for lower ADA levels in older subjects, this did not reach statistical significance, 23.2 v 50.5 respectively.

Conclusion: Patients > 65 years on infliximab are less likely to have suboptimal trough levels on standard dosing regimens. Lower ADA levels suggests a role for immunosenescence in these patients and warrants further investigation.

Disclosure: Nothing to disclose

P0566

THE ANTI IL-23/IL-12 AGENT USTEKINUMAB IS AN EFFECTIVE AND SAFE INDUCTION THERAPY IN PATIENTS WITH CROHN'S DISEASE REFRACTORY OR INTOLERANT TO ANTI-TNF: A MULTICENTRE ITALIAN STUDY

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Introduction: There are limited real-life studies in medical literature evaluating the efficacy and safety of Ustekinumab, an Anti IL-23/Anti IL-12 agent, in patients with Crohn's Disease (CD) who required treatment because of refractoriness or intolerance to previous biological treatments. Thus, the aim of this study was to assess the effectiveness and tolerability of Ustekinumab in anti-TNF refractory or intolerant CD patients.

Aims & Methods: All CD patients who completed induction with Ustekinumab in four Italian IBD Units (Padua, Santorso, Pordenone and Pisa) were enrolled. Patients were evaluated after induction (first intravenous dose followed by a subcutaneous dose at 8 weeks) and clinical (Harvey Bradshaw Index) and bio-chemical data, including fecal calprotectin (FC) and C-Reactive Protein (CRP) were collected. Information on need of optimization (every 12 or 8 weeks) and adverse events were also collected. Continuous and categorical variables were expressed as mean with standard deviation (sd) and frequency with percentages, respectively. Comparisons between variables were conducted using paired t-test and chi-square test. Data were analyzed using STATA11.1 software.

Results: 104 patients were included (63 males, mean age 43 ± sd 13.6 years). All of them had previously been treated with at least one biologic agent and 95.9% with oral steroids. The main indications for starting therapy were: previous treatment failure (79.2%) and pharmacological intolerance (16.8%). At the time of the induction, 29.7% patients were under steroid treatment. Post induction, clinical remission was obtained in 62.3% patients, while steroid-free clinical remission in 50.7%. Moreover, a statistically significant reduction of FC (from 916 ug/L to 444 u/L, p< 0.001) and normalization of CRP (n=14, 33.3%; p< 0.001) were observed. After induction, 3 adverse effects were reported, and in two treatment discontinuations was necessary (i.e. 1 case of pyelonephritis and 1 case of a re-activation of entero-cutaneous fistula). Finally, among 104 patients enrolled, 84 (80.9%) were optimized with a maintenance regimen of 8 weeks sub-cutaneous doses.

Conclusion: Our study shows that Ustekinumab seems to be effective in achieving clinical remission and steroid-free clinical remission after induction in the majority of CD patient despite the refractoriness to anti-TNF treatment. Moreover, the drug appeared safe and well tolerated. On the other hand, treatment optimization to 8 weeks was adopted in most of the patients, in order to guarantee a better outcome.

Disclosure: Nothing to disclose

SAFETY OF INFLAMMATORY BOWEL DISEASE DRUGS DURING PREGNANCY AND BREASTFEEDING: MOTHERS AND BABIES' OUTCOMES (DUMBO REGISTRY)

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Introduction: Prospective registries are necessary to evaluate the safety of IBD treatment during pregnancy and in children in the long term.

Aims & Methods: Our aim is to present the DUMBO registry (ClinicalTrials.gov identifier: NCT03894228). This registry aims to know the risk of serious adverse events during pregnancy and childbirth associated with drug treatment for IBD; to assess the developmental status of children born to mothers with IBD, and to know the relative risk of serious adverse events, the prevalence of malformations and the relative risk of tumours up to 4 years of age in children exposed during pregnancy to drugs for IBD, compared to unexposed children.

Prospective, observational and multicentre registry, which enrolls pregnant women with IBD [Crohn's disease (CD), ulcerative colitis (UC), IBD-unclassified] over 5 years in 65 centres in Spain. Each incident gestation is followed-up during pregnancy, and children born to those mothers are followed-up over 4 years to determine the incidence of serious adverse events (such as alteration of developmental status, infections, neoplasia or any other serious adverse event) during the study period. After being registered, pregnant women are contacted at the end of first, second and third trimester, and one month after delivery. After birth, the mothers are contacted every 3 months to include information about the child development and serious adverse events. The registry was kicked off in September 2019.

Results: A total of 184 pregnancies in 182 women have been included so far. Median age was 35 years (IQR=32-38 years). Fifty-eight percent of patients had CD (53% ileal and 38% ileocolonic location; 11% stricturing and 20% fistulising behaviour; and 23% perianal disease) and 42% had UC (32% extensive colitis and 28% left-sided colitis). Twenty-two percent of patients had undergone surgery due to IBD (16% of patients abdominal surgery). Twelve percent of the pregnancies were achieved by assisted reproductive technology. Ten percent of women were former smokers

during gestation. Nine percent of patients had active disease during pregnancy. With respect to treatments, 46% of patients were not exposed to either immunomodulators or to biologic agents during pregnancy, 21% of patients were exposed to immunomodulators, 25% to biologics in monotherapy and 8% to biologics in combination with immunomodulators. Overall, 55 patients were exposed to biologics during pregnancy: 37 to anti-TNF, 5 to vedolizumab and 13 to ustekinumab. The number of deliveries is 51 so far (2 of them twins): 71% vaginal deliveries and 29% caesarean sections. Eleven percent of pregnancies reported at least one serious adverse event: 4 miscarriages, 1 abortion, 2 threatened abortions, 1 preterm delivery, 1 preeclampsia, 1 preeclampsia risk, 1 pancreatitis due to mesalamine, 2 infections, 1 palpitations, 1 intestinal obstruction, 1 haematemesis, 1 retrochorial haematoma and 1 foetal tachycardia.

Conclusion: The DUMBO registry is a multicentre initiative that attempts to fill the need for information on the safety of drugs for IBD in pregnancy. We expect this registry will provide data on the safety of IBD treatments in pregnancy and breastfeeding, and in the children in the long-term.

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UTILITY OF USTEKINUMAB IN ARTICULAR PATHOLOGY ASSOCIATED WITH CROHN'S DISEASE

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Introduction: Ustekinumab has not been shown in pivotal clinical trials to be effective in treating axial spondyloarthritis, despite the mechanism of action and studies in clinical practice suggest that it may be an effective treatment.

Aims & Methods: Patients with an established diagnosis of Crohn's disease undergoing Ustekinumab treatment for the same for at least 1 year and who had stable follow-up in the inflammatory bowel disease unit of Hospital La Paz in Madrid were included. Patients with non-inflammatory joint pathology and who could bias the interpretation of the results were excluded from the sample.

Results: A total of 31 patients treated with Ustekinumab for Crohn's disease were included, among whom 17 (55%) were women. Regarding the location of Crohn's disease in 4 patients (13%) it was ileal, 5 patients (16%) colica, 18 patients 59% ileocolic and 4 patients (13%) upper. The disease pattern was 45% of the cases (14 patients) B1, 36% (11 patients) B2 and 19% (6 patients) B3.

All included patients had received previous anti-TNF treatment, with ustekinumab being the second line in 20 patients (64%) and the third line in 11 patients (36%). It should be noted that 85% of the sample (26 patients) were in remission from the digestive clinical point of view with Ustekinumab treatment at the time of analysis.

45% of the sample (14 patients) had joint symptoms prior to the start of treatment with Ustekinumab., Of which 46% (6 patients) had axial involvement (30% with combined peripheral involvement) and the remaining 54% (7 patients) exclusive peripheral involvement (57% of large oligoarticular or type I joints).

Among the patients with previous known joint involvement, approximately half of them (54%, 7 patients) had had a good clinical response during treatment with anti-TNF.

After the start of Ustekinumab treatment, only 2 patients (6.5%) suffered joint symptoms, one of them with a previous diagnosis of spondyloarthritis and the other "de novo" (manifested as peripheral arthralgias of large joints).

Conclusion: In our experience, patients with Crohn's disease under treatment with Ustekinumab have good control of the joint symptoms associated with IBD, both in patients with a previous diagnosis and in *de novo* cases (or masked by previous treatment with anti-TNF).

Disclosure: Nothing to disclose

P0569

TREATMENT PATTERNS AMONG PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE RECEIVING BIOLOGIC THERAPY IN FRANCE, GERMANY AND THE UNITED KINGDOM

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Introduction: Inflammatory bowel disease (IBD) is a chronic relapsing condition that includes ulcerative colitis (UC) and Crohn's disease (CD). Biologic therapies are established standard of care treatments for IBD; however, biologics can be expensive and patient access may be limited. As less expensive biosimilars are developed and become increasingly available, it is important to understand the treatment patterns within European practices.

Aims & Methods: This retrospective non-interventional chart review study aimed to characterize patterns of use of biologics, including originator biologics and biosimilars, among patients diagnosed with IBD in France, Germany and the UK. Eligible patients included adults (aged ≥ 18 years) with moderate-to-severe UC or CD who received at least one IBD-related biologic between 1 January 2014 and 18 November 2019. Descriptive statistics were used to summarize the treatment patterns and reasons for switching treatments. Analyses were performed separately for patients with UC and those with CD.

Results: Overall, 593 patients with UC and 425 patients with CD were included, and 14 patients were diagnosed with both. Of these, 587 patients were treated for UC and 417 patients were treated for CD. Combinations of biologic and non-biologic treatments were used as first-line therapy in 14.1% of patients with UC and in 11.5% of patients with CD. Patients with UC who received biosimilars as first-line treatment were more likely to receive combination therapy than those who received originator biologics (23.7% vs 12.7%, respectively). This pattern was also observed in patients with CD, although to a lesser extent (biosimilar vs originator, 13.0% vs 11.2%). The mean duration of first-line treatment was similar between patients with UC and those with CD, ranging from 8.6 to 26.6 months for UC and 8.4 to 31.2 months for CD.

Among patients with UC, anti-tumour necrosis factor (TNF) biologics were more commonly prescribed as first-line therapy than other treatments, and originators were prescribed more often than their biosimilars (adalimumab, 32.2%; adalimumab biosimilars, 0.5%; infliximab, 43.6%; infliximab biosimilars, 12.4%; vedolizumab, 6.3%; golimumab, 3.6%; tofacitinib, 1.4%). Similar patterns were observed in patients with CD (adalimumab, 36.7%; adalimumab biosimilar, 4.1%; infliximab, 36.9%; infliximab

biosimilar, 12.5%; vedolizumab, 5.0%; ustekinumab, 4.8%). Vedolizumab (45.5%) and ustekinumab (32.9%) were the most prescribed second-line biologic treatments for UC and CD, respectively.

Among patients with sufficient [OPG1] follow-up time to be eligible for switching, the proportion of patients who switched biologic treatments was lower among patients with UC ($n = 42/250$, 16.8%) than those with CD ($n = 57/216$, 26.4%). The most common reasons for switching were lack of efficacy (UC, 76.2%; CD, 66.7%) and patient or provider preference (UC, 11.9%; CD, 22.8%).

Conclusion: Anti-TNF originator biologics were the most commonly prescribed first-line biologic treatments for IBD in the three European countries studied. Combinations of biologic and non-biologic treatments were often used as first-line therapies, particularly in patients who received biosimilars. Treatment switching occurred in approximately 20% of patients and was primarily owing to lack of efficacy. These patterns suggest there are opportunities to improve treatment management among patients with IBD.

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THIOPURINE THERAPY IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE: ADVERSE EVENTS AND THIOPURINE METABOLITES

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Introduction: Thiopurines are commonly used as maintenance therapy in paediatric patients with inflammatory bowel disease (IBD). Previous studies have mainly focused on the efficacy of these immunomodulatory agents, while information on the incidence of adverse events (AE) is limited.

Aims & Methods: We aimed to assess the incidence and predictive factors of thiopurine-induced AE resulting in cessation of therapy in a real-life cohort of paediatric IBD patients, related to thiopurine metabolites and

biochemical abnormalities. Secondary aim was to assess the overall drug survival of thiopurines. We performed a retrospective, single-centre study of children diagnosed with IBD between January 1, 2000 - December 31, 2019 and treated with thiopurine monotherapy or in combination with anti-TNF. The incidence of thiopurine-induced AE resulting in cessation of therapy and the overall drug survival of thiopurines were evaluated using Kaplan-Meier analysis. Logistic regression analyses were performed to identify potential predictive factors for the probability of cessation by thiopurine-induced AE. Correlations between thiopurine metabolites and biochemical tests were computed using Spearman rank correlation coefficient.

Results: Of 391 paediatric patients diagnosed with IBD in the study period, 233 patients (162 CD, 62 UC, 9 IBD-U) were prescribed thiopurines (230 azathioprine (AZA), 3 mercaptopurine (MP)), of whom 50 patients (22%) discontinued treatment, at least temporary, due to thiopurine-induced AE (median 57 days after initiation). Twenty-six patients (52%) were rechallenged and 18 of them (70%) could continue with the same drug. Fifteen patients (6%) switched to MP after AZA intolerance and 9 of these patients (60%) did not experience the previously reported AE. No predictive factors for the development of AE were identified. Levels of 6-TGN were inversely correlated with white blood cell ($r = -0.17$, $P = 0.001$) and neutrophil count ($r = -0.18$, $P = 0.004$) and positively correlated with mean corpuscular volume ($r = 0.42$, $P < 0.0005$). A positive correlation was found between 6-MMP levels and alanine aminotransferase ($r = 0.10$, $P = 0.049$) and gamma-glutamyltranspeptidase ($r = 0.15$, $P = 0.040$). Twenty-six percent of children were still on thiopurines after 5 years.

Conclusion: In a real life paediatric cohort approximately 20% of paediatric IBD patients discontinued thiopurine treatment due to AE. A challenge or switch to MP is an effective strategy after the development of AE during AZA monotherapy. Levels of 6-TGN and 6-MMP are associated with biochemical abnormalities. Given only 26% of children were still on thiopurines after 5 years, the role of thiopurines as long term maintenance therapy seems to be limited in daily clinical practice.

Disclosure: Nothing to disclose

P0571

GUT MICROBIAL CHANGES IN RESPONSE TO VEDOLIZUMAB TREATMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Around 50% of the patients with Inflammatory Bowel Disease (IBD) respond to vedolizumab treatment and currently it is difficult to predict which patients will respond favorably. A previous study has identified the potential of the gut microbiota in predicting response to vedolizumab treatment.

Aims & Methods: Here we aimed to investigate this predictive potential and we aimed to identify longitudinal gut microbial changes during vedolizumab treatment and their correlation with clinical response. Therefore, we prospectively collected clinical and response data together with a fresh frozen faecal sample prior to the start of vedolizumab therapy, and 14 weeks after in 50 patients with IBD. Faecal microbiome data was generated using whole-genome metagenomic shotgun sequencing. MetaPhlAn2 and HUMAnN2 were used to annotate individual taxa and microbial path-

ways. Response to vedolizumab treatment was defined at week 14 by a decrease of the disease activity scores (HBI and SSCI) by 3 points or more. The baseline samples were analyzed for differences in alpha diversity, beta diversity, individual taxa, and microbial pathways between responders and non-responders. This information was used to build a prediction model by using random forests, thereby dividing the cohort into 75% training set and 25% test set, and general linear models. Additionally, general linear models were used to assess gut microbial changes during vedolizumab treatment in the paired samples in relation to clinical outcome.

Results: Fifty-four % (27/50) of patients responded favorably to vedolizumab treatment. There were no differences in either alpha and beta diversity in relation to treatment response. On taxonomical level we identified a decreased relative abundance at baseline of the genus *Alistipes* in responders compared to non-responders ($p = 0.0019$, FDR = 0.12). We identified that *Alistipes putredinis* accounted for this abundance difference ($p = 0.018$). One of the top microbial pathways associated to treatment response at baseline was the increase in L-histidine biosynthesis in responders ($p = 0.008$, FDR = 0.27). L-histidine has been previously linked to anti-inflammatory characteristics of the gut microbiome. By introducing the top 3 differentially abundant taxa and pathways in our prediction model, we could predict treatment response with an area under the curve of 0.8. We were not able to replicate taxa or pathways which were identified in a previous study predicting vedolizumab response in IBD. When analyzing the longitudinal paired samples, we identified a decrease of the pro-inflammatory genus *Alistipes* ($p = 0.001$, FDR = 0.04) and an increase of the anti-inflammatory genus *Bifidobacterium* ($p = 0.02$, FDR = 0.13) in the responders compared to the non-responders.

Conclusion: In this prospective study we show the predictive potential of the gut microbiota prior to vedolizumab treatment. Furthermore, we identified differences in gut microbial features at baseline and during vedolizumab treatment in responders and non-responders. These findings will help us understand the role of the gut microbiome in inflammation and in response to vedolizumab treatment.

Disclosure: Nothing to disclose

P0572

IMPACT OF 8 WEEKS TOFACITINIB TREATMENT ON HISTOLOGICAL INFLAMMATION IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC).¹ Histologic changes in the colon mucosa during this treatment have not been studied for tofacitinib. It is essential to document disappearance of residual microscopic inflammation even in endoscopic quiescent disease, given the association of persistent neutrophils in the epithelium and/or lamina propria with risk of clinical relapse.² The primary aim of this prospective study was to assess efficacy of tofacitinib induction treatment at 10 mg twice daily (BID) to reduce histologic inflammation after 8 weeks in UC.

Aims & Methods: The TOFA-histology study (NL6520) is an open-label exploratory study to assess changes in histologic inflammation after 8 weeks of tofacitinib (10 mg BID) in 40 patients with moderate to severe UC. In this

interim analysis, data of 32 patients that completed 8 weeks of follow-up were presented. At baseline, two colonic tissue biopsies were collected from the most affected area between 15 and 30 centimeter (cm) above the anal verge (or < 15 cm in case of proctitis). After 8 weeks (or at early withdrawal) biopsies were taken from the same location. Histologic inflammation was quantified using the Robarts Histopathology Index (RHI) and the Geboes Score (GS) by a blinded inflammatory bowel disease (IBD) pathologist and endoscopic Mayo score was assessed by a blinded IBD gastroenterologist.^{3,4} The RHI-score ranges from 0 to 33 and the GS was transformed to an ordinal GS (range 0-28). An ordinal GS of 16 corresponds to GS grade 3.0 (absence of neutrophils in epithelium). Reduction in histologic inflammation was reported as a median (IQR) decrease in GS and RHI score between baseline and 8 weeks.

Results: Thirty-two patients were included (median age 42±15 years; median disease duration 7 (4-13) years). In total, 5 (16%) patients were biologic naïve, 11 (34%) had failed ≥1 anti-tumor necrosis factor (anti-TNF) agent and 16 (50%) had failed anti-TNF and vedolizumab. At baseline, the median total Mayo score was 10 (9-11); 24 (75%) patients had an endoscopic Mayo score of 3 and 8 (25%) had an endoscopic Mayo score of 2; median ordinal GS and RHI score were 19 (18-26) and 14 (10-21), respectively. After 8 weeks of treatment, a median decrease of 15 (0-21) in ordinal GS and 7 (2-14) in RHI score was observed. After 8 weeks, 23 (72%) patients achieved clinical response, 8 (25%) were in clinical remission, 17 (53%) had endoscopic response, 20 (63%) histologic remission and 10 (31%) histo-endoscopic mucosal healing, respectively (table 1).

Definitions	Description	Total group (n=32)	Anti-TNF naïve (n=5)	Failed anti-TNF (n=27)
Clinical response	Decreased total Mayo score ≥ 3 and ≥ 30% and decreased rectal bleeding subscore ≥ 1 or absolute subscore ≤ 1	23 (72%)	2 (40%)	21 (78%)
Clinical remission	Total Mayo-score ≤ 2, with no individual subscore > 1	8 (25%)	1 (20%)	7 (26%)
Symptomatic remission	Clinical remission and both rectal bleeding and stool frequency subscore = 0	6 (19%)	0 (0%)	6 (22%)
Endoscopic response	Decreased endoscopic Mayo score ≥ 1	17 (53%)	2 (40%)	15 (56%)
Endoscopic improvement	Endoscopic Mayo score ≤ 1	13 (41%)	2 (40%)	11 (41%)
Endoscopic remission	Endoscopic Mayo score = 0	2 (6%)	0 (0%)	2 (7%)
Histologic remission	Absence of neutrophils in epithelium, crypt destruction and erosion and ulcers (GS ≤ 3.0 and RHI-scores 'neutrophils in epithelium' and 'erosion or ulcer' = 0)	20 (63%)	2 (40%)	18 (67%)
Histo-endoscopic mucosal healing	Endoscopic improvement and histologic remission	10 (31%)	2 (40%)	8 (30%)
Deep clinical, endoscopic and histologic remission	Clinical, endoscopic and histologic remission and rectal bleeding subscore = 0	2 (6%)	0 (0%)	2 (7%)

[Table 1. Secondary outcomes after 8 weeks tofacitinib (10 mg BID)]

Conclusion: In this open label exploratory analysis of 32 patients, tofacitinib reduces the inflammatory infiltrate and leads to histologic remission in two thirds of UC patients after 8 weeks of treatment. The proportion of patients with histologic remission was higher than those with endoscopic improvement. This suggests patchy or proximal healing tendency, since biopsies were taken between 15 and 30 cm above the anal verge and the maximum endoscopic Mayo score was determined based on all colon segments visualized.

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P0573

MADCAM-1 ANTAGONISM WITH ONTAMALIMAB PROMOTES DRAINAGE OF LEUKOCYTES *IN VITRO* THROUGH THE INTESTINAL LYMPHATIC ENDOTHELIUM FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Haematic and lymphatic endothelial cells are key regulators of the inflammatory response, which not only act as vessel wall surfaces, but also control the influx and efflux of leukocytes to and from inflamed tissues. In inflammatory bowel disease (IBD), leukocytes bearing the $\alpha 4\beta 7$ integrin selectively bind to the mucosal addressin cell adhesion molecule 1 (MAdCAM-1), which is expressed in the haematic and lymphatic endothelium of the gut. Most of these $\alpha 4\beta 7$ -positive leukocytes are represented by various subsets of CD4⁺ and CD8⁺ T cells, including effector and central memory (CM) T cells, which are known players in perpetuating chronic intestinal inflammation. Inhibiting the binding of $\alpha 4\beta 7$ -bearing leukocytes to MAdCAM-1 with the anti- $\alpha 4\beta 7$ monoclonal antibody vedolizumab is an approved therapy for IBD and the anti-MAdCAM-1 antibody ontamalimab is under clinical investigation in IBD. However, it is not known whether these compounds act only on the influx of inflammatory cells through the haematic endothelium or also on the efflux of leukocytes through lymphatic vessels. We explored the biological effects of ontamalimab, vedolizumab and infliximab on recirculation of human leukocytes through both the haematic and lymphatic intestinal endothelium of patients with IBD.

Aims & Methods: We tested the capability of intestinal haematic cells (HIBEC) and lymphatic (HILEC) endothelial cells isolated from IBD patients to mediate *in vitro* adhesion and transmigration of human leukocytes, using peripheral blood mononuclear cells or lamina propria mononuclear cells, respectively, in the presence or absence of ontamalimab, vedolizumab and infliximab. We evaluated the immunophenotype of adherent and transmigrated cells by fluorescence-activated cell sorting analysis, and tested the direct effects of the three drugs on IBD HIBEC and HILEC, by measuring the expression of adhesion molecules and the alteration of endothelial permeability.

Results: Ontamalimab significantly inhibited the adhesion of CD4⁺ and CD8⁺ effector and CM T cells to the haematic endothelium, more effectively than infliximab and vedolizumab, and at lower concentrations. Furthermore, we showed for the first time that, while infliximab and vedolizumab did not affect adhesion and transmigration of leukocytes to and through

lymphatic endothelial cells, ontamalimab significantly increased the adhesion of $\alpha 4\beta 7$ CD4⁺ naïve and CM T cells to HILEC, and highly induced the transmigration of naïve CD8⁺ and CD4⁺ T cells, and $\alpha 4\beta 7$ ⁺ natural killer cells through the IBD lymphatic endothelium. Interestingly, we provide the first evidence that ontamalimab is the only compound able to directly affect HILEC permeability, in terms of reduced transendothelial electrical resistance, and increased expression of adhesion molecules such as vascular cell adhesion protein-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1).

Conclusion: These findings demonstrate that ontamalimab, contrary to infliximab and vedolizumab, not only blocks the adhesion of inflammatory cells to the haematic endothelium, but also stimulates the trafficking of specific leukocyte subpopulations through HILEC. Our data support the concept that ontamalimab may promote the resolution of intestinal inflammation by directly affecting the permeability of lymphatic endothelial cells, thus improving gut lymph drainage.

Disclosure: This study was funded by Shire, a Takeda company. Silvia D'Alessio and Salvatore Spanò have no conflicts to disclose. Deborah Palliser and Dan Sexton are employees of Shire, a Takeda company. Silvio Danese has served as speaker, consultant and advisory board member for Abbvie, Allergan, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Ferring, Hospira, Johnson and Johnson, Merck, MSD, Mundipharma, Pfizer Inc, Sandoz, Takeda, Tigenix, UCB Pharma, Vifor.

P0574

NON-MEDICAL SWITCHING FROM REFERENCE ADALIMUMAB TO SB5 BIOSIMILAR: A MULTICENTER REAL LIFE EVIDENCE FROM TUSCANY REGION

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Introduction: SB5 is a new Adalimumab (ADA) biosimilar approved in October 2018 for the treatment of many immune-mediated disorders including Inflammatory Bowel Disease (IBD). Since November 2018 Tuscanian local government proposed non-medical switching for all patients on therapy with ADA originator. In the absence of strong direct evidence for IBD patients, physicians decided to limit switching to those in stable clinical remission.

Aims & Methods: The aim of this study is to assess the clinical effectiveness and safety of SB5 in the treatment of IBD in a cohort of patients in stable remission who underwent a non-medical switching from originator and in a cohort of IBD patients naïve to ADA. From November 2018 to December 2019 we collected clinical and demographic data of IBD patients who underwent a non-medical switching from originator ADA to SB5 biosimilar and who were in remission for at least 3 months before the

switch. Clinical remission was defined as an Harvey Bradshaw Index ≤ 4 for Crohn's Disease (CD) and a partial Mayo Score (pMS) ≤ 1 for Ulcerative Colitis (UC). Clinical remission and safety were assessed at 3, 6 and 12 months after the start of SB5 therapy. In a small cohort of patients the ADA serum trough levels (TLs) and anti-drug serum antibodies (ADAs) were assessed just before the switch and at 3 and 6 months after the switch.

Results: We enrolled 146 consecutive patients (91 M), 31 (21.2%) affected by UC and 115 (78.8%) by CD; 48 naïve to ADA, 98 in the switched cohort. In the naïve cohort, during the follow up 46 patients were evaluated at 3 months, 39 at 6 months and 32 at 12 months, showing remission rates of 84.78%, 71.42% and 90.63% respectively. In the switched cohort 95 patients were evaluated at the 3 months, 91 at 6, 80 at 12 months; the remission rates were 97.89%, 93.40% and 88.75% respectively. No difference in terms of clinical remission was observed between the two cohorts at 6 months ($p=0.473$) and 12 months ($p=0.772$); as expected, at 3 months the remission rate was higher in the switched cohort ($p=0.003$), consistent with disease activity in the naïve cohort compared to the switched patients. Pain at the injection site (ISP) was significantly more frequent in the switched cohort ($p=0.001$), while the adverse events, adjusted for ISP, were comparable in the two cohorts ($p=0.576$).

We evaluated the TLs and ADAs in a subgroup of 17 pts: the mean TLs before the switch and at 3 and 6 months were 14.69 (± 7.72), 14.99 (± 7.97) and 14.31 (± 8.03) $\mu\text{g/mL}$ respectively, with no statistically significant difference ($p=0.180$); no patient developed ADAs after switching to SB5.

Conclusion: In our cohort no differences in terms of remission were found between ADA originator and SB5 biosimilar at 6 and 12 months after switching. Safety of originator and biosimilar were comparable except for ISP, that was more common in switching patients, probably due to SB5 excipients although a nocebo effect cannot be excluded.

Moreover, according to our preliminary data, switching did not affect ADA immunogenicity. In conclusion, our results support the effectiveness and safety of SB5 use both in naïve and switched patients.

Disclosure: Nothing to disclose

P0575

REAL WORLD CLINICAL AND ENDOSCOPIC OUTCOMES AFTER ONE YEAR TOFACITINIB TREATMENT IN ULCERATIVE COLITIS

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Introduction: Tofacitinib is approved for the treatment of moderate to severe ulcerative colitis (UC). [1] However, results obtained with clinical trials often differ from real world treatment outcomes. [2] We aimed to evaluate efficacy of tofacitinib treatment up to one year in achieving steroid-free clinical remission and endoscopic improvement and to assess safety, drug survival and predictors of tofacitinib withdrawal.

Aims & Methods: In this observational cohort study we retrospectively included UC patients who received tofacitinib between 2018 and 2019 at a single tertiary inflammatory bowel disease center. Data was collected retrospectively from start of tofacitinib until 60 weeks of follow-up. Clinical disease activity was recorded at outpatient clinic visits using the Simple Clinical Colitis Activity Index (SCCAI) and endoscopic Mayo scores were obtained by local endoscopists. Biochemical response and remission were assessed in patients with elevated baseline C-reactive protein (CRP) and/or fecal calprotectin (FC). Efficacy and safety outcomes were evaluated after 16, 36 and 52 weeks. Patients who permanently stopped tofacitinib were considered non-responders.

Results: Thirty-six patients were included with a median disease duration of 7 (3-14) years. Eighty-nine % of patients failed prior treatment with anti-tumor necrosis factor (anti-TNF) therapy and 42% had failed vedolizumab. Median follow-up and tofacitinib exposure were 57 (44-60) and 47 (12-52) weeks, respectively. Thirty-nine % (12/31 patients) attained combined corticosteroid-free clinical remission (SCCAI ≤ 2) and endoscopic improvement (Mayo-score ≤ 1) at one year. Secondary outcome measures are summarized in table 1.

Biochemical remission was observed in 34% (10/29) of patients at one year. Seventy adverse events (AEs) were observed of which 9 infections (including 2 herpes zoster infections) led to dose reduction or (temporary) drug withdrawal. Permanent drug withdrawal occurred in 14/36 (33%) patients (10 for non-response, 2 for AEs and 1 for mucosal healing) after a median treatment duration of 9 (5-30) weeks. In 60% of patients (21/35) induction dose (10 mg BID) was reduced to maintenance dosing (5 mg BID) after a median time of 16 (11-22) weeks. Dose re-escalation was observed in 41% (9/22) and in 33% (3/9) another dose reduction was achieved. One year drug survival was 60% and anti-TNF failure and elevated baseline FC (≥ 150 mg/kg) were associated with a lower risk of tofacitinib withdrawal (adjusted HR 0.12 (95% CI 0.03-0.43) and 0.10 (0.03-0.38)).

Conclusion: In this refractory UC population, steroid-free clinical remission and endoscopic improvement at one year was found in 39% of patients. Prolonged high-dose tofacitinib induction was often needed to induce remission. Permanent tofacitinib withdrawal was observed in 33% of patients, which was mainly due to non-response within 9 weeks after treatment initiation. Prior anti-TNF failure and elevated baseline FCP levels were associated with a lower risk of drug withdrawal.

Definitions	Description	Week 16, N=36	Week 36, N=35	Week 52, N=31
Clinical response	Drop in SCCAI score ≥ 3 points	22 (61%)	18 (51%)	16 (52%)
Clinical remission	SCCAI score ≤ 2	16 (44%)	12 (34%)	14 (45%)
Steroid-free clinical remission	Clinical remission without corticosteroid use	13 (36%)	11 (31%)	13 (42%)
Endoscopic response	Drop in endoscopic Mayo score ≥ 1 point	16 (44%)	14 (40%)	16 (52%)
Endoscopic improvement	Endoscopic Mayo score ≤ 1	14 (39%)	13 (37%)	14 (45%)
Steroid-free endoscopic improvement	Endoscopic improvement without corticosteroid use	13 (36%)	12 (34%)	13 (42%)
Combined response	Clinical and endoscopic response	15 (42%)	12 (34%)	15 (48%)
Combined clinical remission and endoscopic improvement	Clinical remission and endoscopic improvement	9 (25%)	7 (20%)	13 (42%)
Steroid-free combined clinical remission and endoscopic improvement	Clinical remission and endoscopic improvement without corticosteroid use	8 (22%)	6 (17%)	12 (39%)
Biochemical response	Drop in CRP ≥ 3 mg/L or FC ≥ 100 mg/kg	24/33 (73%)	21/32 (66%)	17/29 (59%)
Biochemical remission	CRP ≤ 5 mg/L or FC ≤ 150 mg/kg	11/33 (33%)	10/32 (31%)	10/29 (34%)

[Outcomes after 16, 36 and 52 weeks tofacitinib treatment]

References: 1 Sandborn WJ, Su C, Sands BE, et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2017;376:1723-36. doi:10.1056/NEJMoa1606910 2 Ha C, Ullman TA, Siegel CA, et al. Patients Enrolled in Randomized Controlled Trials Do Not Represent the Inflammatory Bowel Disease Patient Population. *Clin Gastroenterol Hepatol* Published Online First: 2012. doi:10.1016/j.cgh.2012.02.004

Disclosure: Nothing to disclose

P0576

ONTAMALIMAB(-S) BLOCKS INFLAMMATORY BOWEL DISEASE T CELL ADHESION AND AMELIORATES T CELL-DEPENDENT COLITIS *IN VIVO*

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Introduction: Gut homing plays an essential role in the pathogenesis of inflammatory bowel disease (IBD) and is specifically controlled via the interaction of $\alpha 4\beta 7$ integrin with mucosal vascular addressin cell adhesion molecule 1 (MAdCAM-1), which is almost exclusively expressed on high endothelial venules of the gut. Thus, inhibition of this interaction is a promising target for the treatment of IBD, and phase 3 trials investigating the anti-MAdCAM-1 antibody ontamalimab are currently ongoing. However, the mechanisms of action of anti-adhesion therapies are currently not well understood.

Aims & Methods: The aim of this study was to further elucidate the mechanism of action of ontamalimab. We used dual luciferase-secreted alkaline phosphatase reporter assays and an overexpression approach to study the regulation of MAdCAM-1 expression and factors affecting its shedding, respectively. We performed fluorescence microscopy to study ontamalimab internalization. Using dynamic adhesion assays and rolling assays we investigated the effects of ontamalimab on immune cell interaction with MAdCAM-1 immobilized on capillaries. The mechanisms of the ontamalimab surrogate antibody, MECA-367 (ontamalimab-s) were evaluated in a T cell transfer colitis model using RNA sequencing.

Results: The expression of MAdCAM-1 was induced by TNF, but not by other pro-inflammatory cytokines. Shedding of MAdCAM-1 was increased by TNF, but also by IL-13. After treatment of MAdCAM-1-overexpressing HEK293T cells with fluorescently labelled ontamalimab, the antibody could be detected within the cytosol.

In dynamic adhesion assays, ontamalimab substantially reduced the firm arrest to MAdCAM-1 of CD4⁺ and CD8⁺ T cells, as well as CD4⁺ T cell subsets like naïve CD4⁺ T cells (CD3⁺ CD4⁺ CD62L⁺), from healthy donors and patients with ulcerative colitis or Crohn's disease. Moreover, our data showed a significant reduction of peripheral blood mononuclear cell rolling on MAdCAM-1 upon treatment with ontamalimab.

Following transfer of naïve CD4⁺ T cells to Rag1^{-/-} mice and treatment with ontamalimab-s or isotype control, ontamalimab-s-treated mice lost less weight and had lower endoscopic and histological disease activity scores. Profiling the transcriptome of lamina propria mononuclear cells and total colon tissue by RNA sequencing revealed differential expression of a large number of genes related to leukocyte migration, CD4⁺ and CD8⁺ T cells, as well as T cell-related pro-inflammatory cytokines in ontamalimab-s-treated mice.

Conclusion: TNF seems to be the key inducer of MAdCAM-1 expression and, together with IL-13, promotes shedding of MAdCAM-1 into the blood stream. On a cellular level, ontamalimab seems to induce internalization of MAdCAM-1. Together, these data will be helpful for the interpretation

of soluble MAdCAM-1 levels in serum and its potential use as biomarker. Our adhesion and rolling assay data are the first to provide evidence for the postulated mechanism of ontamalimab on cell trafficking at a functional level. Moreover, *in vivo* data from an experimental colitis model crucially dependent on T cell trafficking confirm this observation and imply that blocking the $\alpha 4\beta 7$ integrin-MAdCAM-1 axis indeed reduces T cell homing, leading to reduced pro-inflammatory signalling in the lamina propria, resulting in improved clinical outcomes.

Taken together, these findings suggest efficacy of anti-MAdCAM-1 therapy in intestinal inflammation and support ontamalimab as a promising candidate for the treatment of IBD.

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P0577

ANTI-TNF SERUM CONCENTRATIONS ARE ASSOCIATED WITH ENDOSCOPIC REMISSION IN CROHN'S DISEASE

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Introduction: There is growing evidence that the approach based on target levels of anti-TNF leads to a more efficient use of the drug and closer monitoring of inflammatory bowel disease (IBD) patients. Also, some studies establish the association between anti-TNF trough levels and mucosal healing in these patients. The aim of this study is to assess whether higher serum concentrations of anti-TNF predict mucosal healing in Crohn's disease (CD) patients.

Aims & Methods: We designed a retrospective study with CD patients receiving anti-TNF, Infliximab and Adalimumab, in both induction and maintenance therapy in a single center in Madrid, Spain. Endoscopic mucosal healing was defined as Single Endoscopic Score for CD (SES-CD) score < 3 and Rutgeerts score < i2 in operated patients. Anti-TNF concentrations were measured using Enzyme-Linked ImmunoSorbent Assay (ELISA) method.

Results: A total of 140 patients were included. 75 (53.6%) were female, 74 (52.8%) under treatment with Adalimumab, and 66 (47.2%) with Infliximab. The median of the anti-TNF concentration was 9.8 µg/mL in patients under treatment with Adalimumab, and 4.6 µg/mL in those with Infliximab. In patients receiving Adalimumab, anti-TNF levels were higher in the group with mucosal healing rather than the group without mucosal healing (11.4 vs 6.2 µg/mL, p=0.07. Although patients with Infliximab presented higher concentrations in the group with mucosal healing (5.1 vs 4.9 µg/mL), differences were not statistically significant (p=0.9). Lower anti-TNF concentrations were associated with postoperative recurrence reaching statistically significance differences in patients with Adalimumab (7.6 µg/mL vs 12.4 µg/mL), p< 0.05.

Conclusion: Higher serum levels of Adalimumab are associated with mucosal healing in CD patients. However, statistically significant differences are not observed in Infliximab. Also, postoperative recurrence is associated with lower anti-TNF trough levels, with a stronger association in the subgroup of Adalimumab.

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Disclosure: Nothing to disclose

P0578

ADALIMUMAB TROUGH LEVELS ARE ASSOCIATED WITH CLINICAL, BIOLOGICAL AND ENDOSCOPIC REMISSION IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Adalimumab is often used in Crohn's disease (CD) patients in order to achieve or maintain remission. Current evidence suggests the association between anti-TNF trough levels with clinical and biological response, as well as mucosal healing, which is known as deep remission in patients with inflammatory bowel disease.

Aims & Methods: We designed a retrospective study in CD patients receiving Adalimumab in both induction and maintenance therapy in a single center in Madrid, Spain. Clinical remission was defined as Crohn's Disease Activity Index < 150. Biological response was assessed considering C-reactive protein (CRP) < 5.0 mg/L and faecal calprotectin < 100 μ g/g. Endoscopic mucosal healing was defined as Single Endoscopic Score for CD (SES-CD) score < 3 and Rutgeerts score < i2 in operated patients.

Results: A total of 74 patients were included. Patients with clinical remission had Adalimumab levels significantly higher than patients who reached clinical response without remission (11.2 vs 6.9 μ g/mL), $p=0.007$. Statistically significant differences were not observed between levels according to CRP ($p=0.3$). Higher levels were observed in patients with lower faecal calprotectin (10.9 vs 6.8 μ g/mL), $p=0.02$. Regarding endoscopic response, levels were higher in patients with mucosal healing than patients with activity (11.4 vs 6.2 μ g/mL), $p=0.07$. Also, anti-TNF concentrations were lower in patients with postoperative recurrence reaching statistically significance (7.6 μ g/mL vs 12.4 μ g/mL), $p=0.046$.

Conclusion: In patients with CD treated with Adalimumab, higher anti-TNF serum levels are associated with clinical remission, biological response with lower faecal calprotectin, and mucosal healing assessed by colonoscopy.

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Disclosure: Nothing to disclose

P0579

TREATMENT OPTIONS IN IBD PATIENTS IN ROUTINE CLINICAL PRACTICE IN RUSSIA, KAZAKHSTAN AND BELARUS - INTERIM ANALYSIS OF THE INTENT STUDY

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Introduction: There are different treatment options available for inflammatory bowel disease (IBD) patients. The aim of the INTENT study, an international, multicenter, non-interventional study [NCT03532932] is to establish treatment patterns used in routine clinical practice for IBD patients in Russia, the Republic of Belarus, and the Republic of Kazakhstan.

Aims & Methods: The study enrolls patients with documented moderate to severe ulcerative colitis (UC)/Crohn's disease (CD) with exacerbations treated by systemic corticosteroids, and/or immunosuppressants, and/or biologics at the time of enrollment or within 2 years before inclusion into the study. We present interim analysis of data collected during 2-year retrospective period from the first 706 enrolled patients. The sequence of treatments or their combinations use over time were considered as a therapeutic pattern.

Results: Present analysis covers retrospective data from 706 patients: 465 (65.9%) patients with UC and 241 (34.1%) patients with CD. In UC patients (but not in CD) the most frequently used treatment was 5-aminosalicylates (5-ASA) as monotherapy or in combination with steroids (25.4%). Equally as often patients with UC and CD received 5-ASA in combination with immunomodulators (IM) and steroids with or without their subsequent

stopping (20.4% and 24.9%, respectively). There was no permanent maintenance treatment either with conventional medications or biologics in 14.8% of UC patients. This pattern was found in only 5% of CD patients. Various patterns with biologics were revealed: 13.6% UC patients and 24.1% CD patients received anti-tumor necrosis factor (TNF) agents in combination with different conventional therapy. Another group of patients received 5-ASA with subsequent addition of anti-TNF agents (18.1% UC patients and 24.5% CD patients). Further these patients continued their treatment with this combination or anti-TNF monotherapy. Vedolizumab with or without conventional therapy was prescribed in 3.4% UC patients and 10.4% CD patients. In 3.4% and 7.5% of UC and CD patients, respectively, treatment with biologics was stopped for different reasons and patients continued conventional treatment only.

Conclusion: INTENT interim analysis demonstrated low use of biologics in patients with moderate-to severe IBD in Russia, Kazakhstan and Belarus. It was also revealed a high frequency of steroids use in all treatment patterns. Some of UC and CD patients do not receive any maintenance IBD treatment. Overuse of 5-ASA in CD patients and unjustified continuation of 5-ASA in combination with biologics also claims an attention.

Disclosure: The study and presented analysis were sponsored by Takeda.

P0580

GRANULOCYTE AND MONOCYTE APHERESIS IS AN EXCELLENT CHOICE AS AN ADJUNCTIVE THERAPY TO INDUCE AND MAINTAIN REMISSION IN ULCERATIVE COLITIS: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: The goal of treatment in ulcerative colitis (UC) is to induce and maintain remission. The addition of granulocyte and monocyte apheresis (GMA) to conventional therapy may be a promising therapeutic alternative.

Aims & Methods: In this meta-analysis, we aimed to assess the efficacy and safety profile of GMA as an adjunctive therapy. We searched four databases (PubMed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials) for randomized or minimized controlled trials which discussed the impact of additional GMA therapy on clinical remission induction and clinical remission maintenance compared to conventional therapy alone. Primary outcome were clinical remission induction and maintenance, secondary outcomes were adverse events and steroid-sparing effect. Odds ratios (OR) with 95% confidence intervals were calculated. Trial Sequential Analyses (TSA) were performed to adjust for the risk of random errors in meta-analyses.

Results: A total of eleven studies were eligible for meta-analysis. GMA was clearly demonstrated to induce and maintain clinical remission more effectively than conventional therapy alone (598 patients: OR: 1.93, CI: 1.28-2.91, p=0.002 for induction; 71 patients: OR: 8.34, CI: 2.64-26.32, p< 0.001 for maintenance).

Conclusion: GMA appears to be more effective as an adjunctive treatment in inducing and maintaining remission in UC patients than conventional therapy alone.

Disclosure: Nothing to disclose

P0581

PRELIMINARY EXPERIENCE IN MAINTENANCE TREATMENT WITH INTRAVENOUS USTEKINUMAB AS A RESCUE FOR LOSS OF RESPONSE TO SUBCUTANEOUS DOSES

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Introduction: Ustekinumab (UST) is an effective biological therapy for induction and maintenance of remission in patients with Crohn's disease (CD). It requires a weight-adjusted intravenous (IV) induction dose followed by periodic subcutaneous (SC) doses of 90 mg (1). However, a significant number of patients are unresponsive or experience a secondary loss of response (2). It has been suggested that higher levels of UST may be associated with better clinical response rates (3,4), so it is also plausible to think that the administration of IV UST as maintenance treatment may increase bioavailability and thus combat a primary or secondary loss of response.

Aims & Methods: We propose that the change to maintenance UST IV could serve as a rescue in patients with moderate-severe CD who present loss of response to UST SC.

We present a series of cases of CD that after presenting partial response or loss of secondary response to treatment with UST SC are rescued by changing the maintenance pattern to weight-adjusted doses of UST IV.

Results: We presented 6 adult patients (>18 years), with moderate-severe CD. The 83.3% (5/6) had a history of at least one previous surgery in relation to their CD. The median time of evolution since the diagnosis of the disease was 10 years (IQR 3.5-13.5). We observed ileal involvement in 33.3% (2/6), colonic in 16.7% (1/6) and ileocolonic in 50% (3/6). 83.3% (5/6) patients had associated perianal disease (Table 1).

One patient received UST after failure of a single anti-TNF, the rest had failed at least two biological treatments.

The median time between initiation of UST and change of subcutaneous to intravenous and weight-adjusted maintenance dose was 5.5 months (IQR 1.75-10.25).

At the beginning of rescue treatment with weight-adjusted IV dose we found: Harvey's index mean value of 7 (IQR 5-10), PCR and fecal calprotectin (FPC) mean value of 14 mg/L (IQR 9.75-18.5 g/L) and 1040 mcg/g (IQR 248.25-1939.25 mcg/g) respectively. While at 8 weeks after the first maintenance dose iv the mean value of Harvey's index was 3.17 (IQR 2-4.25) and the mean PCR and CPF were 5.18 mg/L (IQR 4.25-6.57 g/L) and 150.33 mcg/g (IQR 34-384 mcg/L).

We observed a decrease in CRP in 100% of cases, and a decrease in CPF in 5 patients after treatment with UST. In the only case that there was no decrease in CPF, it went from 22mcg/g to 66mcg/g (within the range of normal in IBD), and is one of the cases of ileal affectation, so we could consider it less representative. It should be noted that no adverse effects have been recorded to date.

Conclusion: Treatment with UST has been a great alternative for those patients with CD who present primary or secondary failure to anti-TNF (5), although a percentage of patients present partial response or loss of response to the usual UST pattern (6). Maintenance with UST IV could be

an option to consider, and more evidence is needed to support the usefulness of maintenance IV administration, as well as to evaluate whether the associated serum level determination could be a tool to assist this therapeutic option.

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Disclosure: Nothing to disclose

P0582

TREATMENT-BASED RISK STRATIFICATION OF INFECTIONS IN INFLAMMATORY BOWEL DISEASE: A COMPARISON BETWEEN ANTI-TNF α AND NON-BIOLOGIC EXPOSURE IN REAL WORLD SETTING

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Introduction: Infective issues about anti-TNF α agents in inflammatory bowel disease (IBD) remain controversial, especially when compared with non-biologic treatments.

Aims & Methods: to evaluate the incidence and prevalence of several viral, bacterial and fungal infections in anti-TNF α -exposed patients compared to non-biologic treatments.

All naïve IBD subjects treated with anti-TNF α and matched non-biological-exposed patients were included. We evaluated incidence and prevalence of infections in the two populations, the rate of serious infections, the differences in infection rate between drugs and the predictors of infection in anti-TNF α -exposed subjects.

Results: Among 3453 patients in the database, 288 anti-TNF α -exposed subjects and 288 non-biologic-exposed IBD controls met inclusion criteria and were enrolled. Fifty-eight infections (20.1%) occurred during anti-TNF α treatment vs 23 (8%) in the matched group (OR 2.9, $p < 0.001$) (incidence 5.72 vs 0.96/100 patient-years respectively, incidence ratio (IR) 6, $p < 0.001$). IR was higher for anti-TNF α vs mesalamine/sulphasalazine (IR 40.8, $p < 0.001$), similar to azathioprine/6-mercaptopurine/methotrexate (IR 0.78, $p = 0.32$) and lower than oral corticosteroids exposure (IR 0.05, $p < 0.001$). The incidence rate of serious infections was 1.3 in the anti-TNF α -exposed vs 0.38/100 patient-years in non-exposed subjects

(IR 3.44, $p = 0.002$), without significant difference between anti-TNF α and azathioprine/6-mercaptopurine/methotrexate (1.3 vs 3.03/100 patient-years, IR 0.43, $p = 0.1$). Predictors of infections in anti-TNF α -exposed patients were concomitant use of systemic steroids (OR 1.9, $p = 0.02$) or azathioprine (OR 2.6, $p = 0.01$) and a BMI < 18.5 at time of infection (OR 2.2, $p = 0.01$).

Conclusion: The risk of developing infections during anti-TNF α therapy remains high, although not dissimilar to that found for other immunosuppressants, while concomitant immunosuppression and malnutrition appear the most important causes of infection.

Disclosure: Nothing to disclose

P0583

SWITCHING FROM ADALIMUMAB ORIGINATOR TO ABP 501 BIOSIMILAR: A MULTICENTRIC NORTH ITALIAN STUDY

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Introduction: In late 2018, adalimumab (ADA) biosimilars have been approved by the EMA with the same indications of the reference product (RP), that is Humira. However, while their efficacy and safety have been proven in patients with rheumatoid arthritis and psoriasis showing no differences compared to the RP, data on inflammatory bowel disease (IBD) is lacking. The primary aim of this study was to verify the ability of ABP501 to maintain the clinical response induced by the RP after switching to the biosimilar.

Aims & Methods: We retrospectively enrolled all consecutive patients who switched to ABP501 by ADA Originator at the IBD Units of Veneto Region (Padua, Santorso) from December 2018 to November 2019. We collected data on partial Mayo (p-Mayo) Score, Harvey-Bradshaw Index (HBI), C Reactive Protein (CRP), fecal calprotectin (FC), concomitant steroid and azathioprine therapy at the time of the switch (T_0) and after six months. Continuous and categorical variables were expressed as mean with standard deviation (SD) and frequency with percentages respectively. Comparisons among variables were conducted using one-way ANOVA and Chi-square. Data were analyzed using STATA11 software.

Results: Fifty-eight IBD patients switched to biosimilar [12 with Ulcerative Colitis (UC) and 46 with Crohn Disease (CD)] were included in the study. All switched patients were in remission or in mild clinical activity at the time of the switch. We observed a clinical worsening and clinical improvement in 12 and 3 patients, respectively ($p = 0.001$) from T_0 to T_1 . FC value increases at T_1 compared to T_0 (from a mean value of 98.32 to 137.9 $\mu\text{g/g}$) but without significantly difference. Ten patients needed to add steroids at T_1 ($p = 0.04$) and eight (13,7%) needed therapeutic optimization. Finally, 11 (18,9%) patients stopped therapy: 10 for loss of response and 2 for adverse event.

Conclusion: Our data shows that after switching, 1/3 of the patients may experience a disease relapse, requiring treatment optimization (i.e. addition of steroids or increasing the dose to once a week) or treatment discontinuation. Thus, patients should be strictly observed in order to prevent or, at least, early manage such clinical relapses. Larger and longer studies are mandatory to understand the clinical implications of these findings.

Disclosure: Nothing to disclose

P0584

TREATMENT OF SYMPTOMS IN THE ABSENCE OF INFLAMMATION IN INFLAMMATORY BOWEL DISEASE (TRAIN-IBD): INTERIM RESULTS

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Introduction: Irritable Bowel Syndrome (IBS) is prevalent in the general population, estimated at 5-20%, but may have a prevalence as high as 35% in quiescent Inflammatory Bowel Disease (IBD). This subset of IBD patients consistently report lower quality of life with increased anxiety and depression. Probiotics have been explored as a treatment option for IBS and active IBD separately with mixed results to date. However, no trials have examined the use of probiotics for IBS/IBD overlap.

Aims & Methods: This was a randomised controlled trial to assess the efficacy of probiotics in reducing IBS symptoms for patients with IBD in remission. IBD patients were recruited from out-patient clinics at an academic teaching hospital in Dublin. Inclusion criteria required were an established diagnosis of IBD considered to be in remission as defined by a C-reactive protein (CRP) less than 5mg/L and a faecal calprotectin (FCP) less than 250µg/g at week 0. All patients also met Rome IV Criteria for a diagnosis of IBS. They were randomised to receive either placebo or a probiotic containing *L. rhamnosus*, *E. faecium*, *L. acidophilus*, and *L. plantarum*. All participants returned after 12 weeks for further assessment of symptoms, repeat CRP and FCP. Quality of life data was collected at week 0 and week 12 including the IBS Symptom Severity Scale (IBS-SSS), Short IBD Questionnaire (SIBDQ) and Patient Health Questionnaire (PHQ-15).

Results: Eighteen patients have completed 12 weeks of treatment with placebo or probiotic to date. Baseline data was collected for all patients with follow up data available for 14. Included in this group are 5 Ulcerative Colitis (UC) patients and 9 Crohn's disease (CD) patients. Harvey Bradshaw Index (HBI) was calculated for all CD patients and Partial Mayo Score was used for UC patients (Table 1). Average SIBDQ score was 35 and 36.3 at baseline in the treatment and placebo group respectively. Higher SIBDQ scores at week 12 were suggestive of improvements in disease related quality of life (Table 1). Lower scores were found in all groups for IBS-SSS and PHQ-15 indicating improved quality of life (Table 1), though numbers were too small to draw statistical significance from these findings.

	Total population (n=18)	Probiotic Total (n=8)	Placebo Total (n=6)	CD Probiotic Group (n=5)	CD Placebo Group (n=4)	UC Probiotic Group (n=3)	UC Placebo Group (n=2)
IBS-SSS Week 0	47.4±17.1	53±21.3	47.6±12.6	51	46.6	56	49.7
IBS-SSS Week 12	40±20.4 (n=14)	43±26.2	37.3±9.9	45	37.1	40	37.5
SIBDQ Week 0	36.9±8.7	35±11.9	36.3±3.1	37.3	27.8	32	39.5
SIBDQ Week 12	41.8±10.2 (n=14)	43.4±12.5	40.0±7.4	41.2	40.3	49	39.5
PHQ 15 Week 0	14.2±3.5	13.8±2.6	16.2±4.4	13.6	14.3	14	19
PHQ 15 Week 12	13.2±4.1 (n=14)	12.5±3.3	14.2±5.2	13.4	12.0	11	18.5
Partial Mayo Score/HBI week 0:	9.2	3.8	2	2.5			
Partial Mayo Score/HBI week 12:	7	4.8	3	0.5			

[Table 1: Average scores at week 0 and 12 for patients in the probiotic (treatment) group and placebo group.]

Conclusion: Despite evidence of remission, poor disease related quality of life was observed in this IBD/IBS overlap group highlighting a pressing need for interventions to address quality of life issues in this cohort. The data suggests a trend towards improved quality of life for all participants, however, similar results were obtained in the active intervention and placebo groups. More data is required in order to assess for significance.

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Disclosure: Nothing to disclose

P0585

LONG-TERM OUTCOME OF PATIENTS WITH SEVERE ULCERATIVE COLITIS AFTER RESCUE-THERAPY WITH CYCLOSPORINE A

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Introduction: Although the early outcomes of ulcerative colitis (UC) after a rescue therapy with Cyclosporine A (CyA) are known, data of long-term disease evolution are scarce.

Aims & Methods: Our aim was to evaluate long term clinical outcomes of patients with severe attack of UC after rescue therapy with CyA.

All episodes of patients with active UC admitted to Tampere University hospital between December 2006 and January 2020 were identified and reviewed from patient records. Only patients treated with CyA were included.

Results: Total of 182 patients were included in this study. Males accounted for 51 % (93) of patients with median age of 32 years (range 16-66 years) at index flare.

In this series 76 % (139) responded to CyA, thiopurines were used as maintenance therapy. After median follow-up of 3.8 years (range 0.7-13.1 years), 23 % (32) of the responders were in long-term remission with no need for further corticosteroids, rehospitalization or enhancement of pharmacotherapy. One third (43) of patients with initial response to CyA eventually needed surgery in long-term follow-up.

Sixty-three per cent (27) of the patients not responding to CyA had emergency colectomy. 37 % (16) of the non-responders had infliximab as second-line rescue therapy of which 69 % (11) needed surgery within follow-up.

Of all the patients 46 % (84) needed corticosteroids for relapse, 30 % (55) were re-hospitalized and 32 % (58) needed further enhancement of treatment with Infliximab. Total of 15 % (28) of patients had emergency colectomy. Overall colectomy rate was high up to 45 % (81), median time from treatment to colectomy 1.15 years (range 0.01-5.3 years), respectively.

Conclusion: Although 76 % of patients had initial response to Cyclosporine A substantial proportion of patients needed further therapy and almost half of all patients were operated within long-term follow-up.

Disclosure: Nothing to disclose

P0586

THE EFFECTS OF COVID19 ON IBD PRESCRIBING AND SERVICE PROVISION

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Introduction: There are limited data on the effect of COVID19 on inflammatory bowel disease (IBD) service provision and prescribing practices.

Aims & Methods: We aimed to quantify the effects of COVID19 on our IBD service. This included evaluation of service provision, prescribing practices and use of therapeutic drug monitoring (TDM). This is a single centre retrospective observational cohort study. We extracted data from our local IBD databases, electronic patient records and radiology and endoscopy reporting systems between 16/3/20-17/4/20 and the corresponding period in 2019. To evaluate differences in prescribing practices we compared treatment decisions, made for patients with active disease in our biologic and immunosuppressant multidisciplinary meeting. We then reviewed the characteristics of patients who had been commenced on, or had switched, biologic therapy. To compare these cohorts we used Fisher's exact test for categorical data and Mann-Whitney test for continuous variables. Descriptive statistics were used for prescribing practices and service provision.

Results: Amongst patients initiating IBD therapy, a higher proportion were commenced on biological therapy during COVID19 compared with pre-pandemic (29/45, 64% vs 19/50, 38%). We compared characteristics of patients commencing on or switching biologic therapy pre-COVID19 (n=37) and during COVID19 (n=36). The cohorts had similar IBD phenotypes, age of onset as well as disease extent/distribution. In the pre-COVID19 cohort the median age was higher (36 vs 29 years, p=0.02) and median disease duration was longer (9.3 vs 5.2 years respectively, p=0.009). During COVID19 there was an increase in the proportion of patients receiving vedolizumab (22% vs. 39%), adalimumab (19% vs 25%) and ustekinumab (24% vs 28%), while infliximab and tofacitinib prescribing fell (14% vs 3% and 8/37 vs 2/36 respectively). Across all biologic classes there was a reduction in concomitant immunomodulator prescribing and a tendency towards prescribing biologics in immunomodulator-naïve patients. New prescriptions of thiopurines for any indication fell by 96% (28 vs 1). During COVID19 there was a preference for vedolizumab or ustekinumab compared to the preceding year (24/36, 67% vs. 17/37, 46%) and this cohort was more likely to be TNF-naïve 18/24 (75%) vs. 3/17 (18%) pre-pandemic.

Use of TDM fell by 75% during the pandemic (240 vs. 59 tests pre- and during pandemic respectively). Values for thiopurine metabolites and anti-TNF levels pre- and during COVID19 were 143 vs. 44 samples and 97 vs. 15 samples respectively.

The number of patients seen in outpatient clinics was reduced by 68%. Similarly, the number of MRI scans, lower gastrointestinal endoscopies or abdominal operations fell by 87%, 85% and 100% respectively. Conversely, clinical nurse specialist and pharmacy helpline contacts increased by 76% and 300% respectively.

Conclusion: We observed prescribing differences during COVID19, bypassing the initiation of immunomodulators and/or anti-TNF therapy for active disease in favour of newer biologic agents, predominantly as monotherapy. Judging by the difference in disease duration between the two cohorts, there appeared to be a shift to earlier prescription of biologics. We also observed a rapid reorganisation of service provision that included a shift towards telemedicine and online solutions.

	Total prescriptions pre-COVID19 N=37	Total prescriptions during COVID19 N=36	Biologic prescribed as monotherapy pre-COVID19	Biologic prescribed as monotherapy during COVID19	Thiopurine naïve pre-COVID19	Thiopurine naïve during COVID19	Anti-TNF naïve pre-COVID19	Anti-TNF naïve during COVID19
Adalimumab	7 (19)	9 (25)	1/7 (14)	9/9 (100)	1/7 (14)	5/9 (56)	5/7 (71)	7/9 (78)
Infliximab	5 (14)	1 (3)	0/5 (0)	1/1 (100)	1/5 (20)	0/1 (0)	2/5 (40)	0/1 (0)
Vedolizumab	8 (22)	14 (39)	3/8 (38)	11/14 (79)	1/8 (13)	5/14 (36)	2/8 (25)	9/14 (64)
Ustekinumab	9 (24)	10 (28)	3/9 (33)	10/10 (100)	0/9 (0)	4/10 (40)	1/9 (11)	9/10 (90)

[Number and proportion of patients prescribed biologic therapy before and during COVID19 pandemic (excluding tofacitinib figures), n (%)]

Disclosure: Peter Irving; AbbVie, Celgene, Falk Pharma, Ferring MSD, Janssen, Pfizer, Takeda, Tillotts, Sandoz, Shire, Warner Chilcott: Speaking / education, intermittent - last 3 years. MSD, Pfizer, Takeda: Research, intermittent - last 3 years. AbbVie, Arena, Genentech, Gilead, Hospira, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Prometheus, Roche, Sandoz, Samsung Bioepis, Takeda, Topivert, VH2, Vifor Pharma: Advisory fees, intermittent - last 3 years SH: has received speaker fees from Pfizer, Janssen and Takeda and meeting support fees from Pfizer, Janssen, ViforPharm, Dr Falk Pharma and Ferring JC: hospitality from Janssen, Ferring and Takeda and speaker fees from Takeda RL: has received educational grants from Ferring, Pfizer and Vifor Pharma

P0587

FATIGUE PERCEPTION DURING VEDOLIZUMAB THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES IS ASSOCIATED WITH THERAPEUTIC RESPONSE

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Introduction: Vedolizumab (VDZ) is currently a widely used therapeutic option for patients with moderate-severe ulcerative colitis (UC) and Crohn's disease (CD). Fatigue is a common and aggravating symptom in these patients, which negatively affects their quality of life. An analysis of fatigue perception during VDZ therapy was never been performed.

Aims & Methods: The aims of this study were to evaluate if fatigue perception could be reduced during VDZ therapy and if it could be associated with therapeutic response.

All patients who started VDZ at Pisa University Hospital were prospectively included in this study.

At baseline, at week 14 and at week 54, fatigue perception was evaluated by the administration of Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) questionnaire, whereas quality of life with Inflammatory Bowel Diseases Questionnaire (IBD-Q). At the same timepoints, clinical

activity was assessed in terms of Partial Mayo Score (PMS) for UC and Harvey-Bradshaw Index (HBI) for CD. To evaluate therapeutic effectiveness, all patients performed a colonoscopy at week 54, to assess mucosal healing (MH), defined as a Mayo Endoscopic Score < 2 for UC and as the disappearance of ulcers for CD. Data are shown as mean $\pm$ SEM. Repeated measures were analyzed by two-way ANOVA followed by post-hoc pairwise comparisons. Correlations were tested by Pearson correlation. Logistic regression analysis was used to estimate the likelihood of achieving MH for each FACIT-F point increase at week 14.

Results: We enrolled 57 patients, 39 (68%) with UC and 18 (32%) with CD. FACIT-F values indicated severe fatigue (score < 30 out of 52) at baseline in 32 (56%) patients and increased on average by 6 points (21%) during the study period (time effect, $p < 0.0001$). FACIT-F positively correlated with IBD-Q scores at each timepoint (baseline: $r = 0.76$, $p < 0.0001$; week 14: $r = 0.79$, $p < 0.0001$; week 54: $r = 0.86$, $p < 0.0001$), and negatively correlated with PMS and HBI at week 14 ($r = -0.68$, $p < 0.0001$ and $r = -0.61$, $p = 0.006$, respectively) and at week 54 ($r = -0.76$, $p < 0.0001$ and $r = -0.59$, $p = 0.01$, respectively). Baseline FACIT-F values were similar in patients who achieved MH compared with those without MH ($p = 0.25$). However, patients with MH displayed greater improvements in FACIT-F scores over time (time $\times$ group effect, $p < 0.0001$), so that their scores were significantly higher at week 14 (+6 points, $p = 0.009$) and at week 54 (+12 points, $p < 0.0001$), in comparison with patients not achieving MH. Interestingly, higher FACIT-F values at week 14 were able to predict MH at week 54 (OR 1.13 [1.04-1.14] for each point increase, $p = 0.003$).

Conclusion: VDZ therapy is able to reduce significantly fatigue perception in patients with inflammatory bowel diseases. Assessing FACIT-F at week 14 seems to be reliable in predicting VDZ effectiveness, paving the way for an increasing use of this questionnaire in clinical practice.

Disclosure: Nothing to disclose

P0588

EFFICACY AND SECURITY OF USTEKINUMAB: OUR EXPERIENCE

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Introduction: Crohn's disease is an entity with wide clinical variability, which mainly affects the gastrointestinal tract. There are a broad variety of treatments, being the most recent ones biological therapies. One of them is ustekinumab, which has improved the quality of life of many patients.

Aims & Methods: Our objective is to analyze the baseline situation of 60 patients undergoing treatment with ustekinumab in our center and the evolution of clinical and analytical parameters at 12, 24 and 52 weeks.

60 patients currently receiving ustekinumab treatment with indication of Crohn's disease at Virgen de las Nieves Hospital were selected. Clinical response was analyzed according to the Harvey-Bradshaw Index (HBI) (clinical remission < 5, clinical response decrease ≥ 3 points above the baseline), blood and stool test (CRP, albumin, haemoglobin and calprotectin) at weeks 12, 24 and 52, need for surgery and safety profile.

Statistic analysis was performed using R Commander, by parametric and non-parametric tests, based on usual applicability criteria.

Results: According to HBI, clinical response was obtained in 39.22%, 52% and 60% of patients at weeks 12, 24 and 52, clinical remission in 37.25%, 40.48% and 50% respectively.

Comparing with baseline, HBI (6, 5, 4.5) and Hb (13.3, 13.5, 13.9) showed a statistically significant improve in their values at weeks 12, 24, 52; CRP at week 24, 52 (7.1, 4.35) and calprotectin only at week 12 (653.5).

5 patients needed surgery after beginning ustekinumab (8.33%). 55 patients (91.67%) continue with the treatment, 2 left because of extraintestinal disease, 2 because of non-response and 1 died (unrelated with the treatment). 2 patients (3.45%) suffered mild adverse events (cutaneous). Penetrating disease was associated with statistically significant differences in clinical response according to HBI (38.9% vs 13.3% vs 61.1%; $p = 0.0198$). The only factor significantly associated with greater response at week 52 was previous response at week 12 (83.3% vs 43.8%; $p = 0.0338$).

Age (mean)	45.2 $\pm$ 14.14
Sex (woman)/smoker, n (%)	34 (56.67) / 15 (25)
Montreal, n (%)	A1: 4 (6.67); A2: 43 (71.67); A3: 13 (21.67) L1: 20 (33.33); L2: 9 (15); L3: 31 (51.67); L4: 4 (6.67) B1: 20 (33.33); B2: 18 (30); B3: 22* (36.67); p: 20 (33.33) *Enterointestinal 12 (54.54), enterocutaneous 6 (27.27), enterovaginal 2 (9.09), enterovesical 2 (9.09)
Extraintestinal manifestations, n=27 (45%)	Rheumatological 18 (35.29) - Peripheral (n=8), axial (n=7), both (n=3) Dermatological 13 (25.49) - Psoriasis (n=6), hidradenitis suppurativa (n=2), cutaneous Crohn's disease (n=3), erythema nodosum (n=1), pyostomatitis vegetans (n=1)
Previous surgery, n (%)	37 (61.67) - Ileal resection 17 (45.95), ileocolic resection 12 (32.43), colonic resection 4 (10.81), others 4 (10.81)
Time of disease evolution (months), (median) (IQR)	131.5 (IQR 69.75-233.25)
Corticoid dependence/corticorefractory, n (%)	31 (51.67) / 5 (8.33)
Previous treatment, n (%)	Immunomodulators (IM): 55 (91.67) - thiopurines 50 (90.91), methotrexate 11 (20) Anti-TNF: 56 (93.33) - 1: 19 (33.93); 2: 34 (60.71); 3: 3 (5.36) Vedolizumab: 5 (8.33)
Indication, n (%)	Primary anti-TNF failure 4 (23.33), secondary anti-TNF failure 24 (40), adverse anti-TNF events 13 (21.67), anti-TNF contraindication 6 (10), extraintestinal disease 3 (5)
Concomitant treatment, n (%)	IM 10 (16.67), CTC 15 (25), IM + CTC 2 (3.33)
Intensification (< 8 weeks) / endovenous re-induction, n (%)	11 (18.33) / 4 (6.67)

[Baseline parameters and characteristics of ustekinumab treatment]

Conclusion: In this group, potentially difficult to treat, ustekinumab achieves clinical response in 39.42%, 52.38%, 60% at week 12, 24 and 52. In pivotal study UNITI-1, 50.6% of patients who received the induction dose had previously been treated with ≥ 2 anti-TNF, 66.07% in our group. In our cohort, 28.33% of patients received corticosteroids concomitantly when treatment started vs. 43.3% at UNITI-1. Despite these differences against our group, clinical response and remission data are similar and improve with more weeks of treatment. Prospective studies with bigger sample size would be interesting to confirm it.

Based on our data, ustekinumab seems to be an effective treatment in Crohn's patients, particularly in penetrating disease, with an increase in long term response and a good security profile.

References: Feagan BG, et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med 2016;375:1946-60.

Disclosure: Nothing to disclose

P0589

SAFETY, PHARMACOKINETIC, BIOMARKER, HISTOLOGIC, AND RECTAL BLEEDING ACTIVITY FOLLOWING TREATMENT WITH THE GUT-TARGETED, PHD-INHIBITOR AND HIF-1 α STABILIZER GB004 IN A PHASE 1B TRIAL IN MILD-TO-MODERATE ULCERATIVE COLITIS

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Introduction: GB004 is a gut-targeted small molecule inhibitor of prolyl hydroxylases (PHDs), key enzymes involved in degradation of hypoxia-inducible factor (HIF-1 α), a transcription factor involved in protective cellular responses at the intersection of hypoxia and inflammation. In animal models of inflammatory bowel disease (IBD), PHD inhibition stabilizes HIF-1 α to increase expression of molecules involved in supporting epithelial integrity and barrier function, promoting mucosal healing (MH). GB004 is being developed as an oral treatment for IBD. In healthy volunteers, GB004 showed a gut-targeted pharmacokinetic (PK) profile.

Aims & Methods: We aimed to evaluate the safety, tolerability, and PK and explore the pharmacodynamics and clinical activity of GB004 in adults with active ulcerative colitis (UC). In this double-blind, placebo-controlled, Phase 1b study, subjects were randomized 2:1 to GB004 120 mg solution or placebo once daily for 28 days.

Eligible subjects had histologic activity defined by Robarts Histopathology Index (RHI) ≥ 4 with neutrophils in the epithelium, Mayo endoscopic sub-score (MES) ≥ 1 , and blood in the stool, despite treatment with 5-ASA. RHI and MES were assessed by blinded central reading. Colonic biopsies of the sigmoid and rectum were obtained at screening and Day 28. MH was defined as MES improvement (0 or 1; 0 if screening 1) and histologic remission (RHI ≤ 3 with lamina propria neutrophils and neutrophils in epithelium sub-scores of 0).

Results: Thirty-four subjects were randomized to GB004 (n=23) or placebo (n=11). Mean age (45.4 years), total Mayo score (7.5), sigmoid MES (2.2), and sigmoid RHI (14.1) at baseline were consistent with moderately active UC. The most frequent adverse events in GB004 were nausea (22%) and dysgeusia (13%), all of which were mild in severity except for one report of moderate nausea. One GB004-treated subject discontinued due to lack of efficacy (worsening of UC unrelated to GB004). No effect on plasma erythropoietin or vascular endothelial growth factor was observed. GB004 concentrations were higher in colon tissue vs. blood on Day 28 biopsy.

Preliminary microarray-based mRNA profiling of epithelial gut biopsies showed increased expression of both TJP1 and CLDN1, genes consistent with enhanced epithelial barrier function, and other trends associated with HIF-1 α stabilization in GB004 vs. placebo. Initial results from myeloperoxidase staining suggest a reduction in gut epithelial neutrophil activity vs. placebo.

The proportion of subjects achieving clinical activity outcomes of interest at Day 28 were higher for GB004 versus placebo: histologic remission in sigmoid or rectum (43% vs. 18%); MH in sigmoid or rectum (17% vs. 0%); clinical response (30% vs 18%); and rectal bleeding improvement (62% vs 45%), with percent decrease from baseline of 65.8% vs. 22.7%. One GB004 patient achieved clinical remission at Day 28 vs. no placebo patients.

Conclusion: GB004 was well tolerated over 28 days and demonstrated a gut-targeted PK profile. GB004 showed gene expression reflective of target engagement and enhancement of barrier function in colonic biopsies. Signals of clinical activity were observed for GB004 vs placebo, including histologic endpoints. A phase 2 clinical trial in UC will be initiated in 2020 with alternative GB004 oral formulations that are currently in development. Sponsored by GB004, Inc., a wholly owned subsidiary of Gossamer Bio, Inc.

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P0590

EVALUATION OF SYMPTOM IMPROVEMENT DURING INDUCTION IN PATIENTS WITH CROHN'S DISEASE TREATED WITH MIRIKIZUMAB

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Introduction: Mirikizumab (miri), a humanized, IgG4 monoclonal antibody that targets IL23, has shown efficacy and safety in patients treated for Crohn's disease (CD), psoriasis, and ulcerative colitis. In a phase 2, randomised, parallel-arm, placebo-controlled study, symptom improvement was evaluated in patients with moderately-to-severely active CD after intravenous induction treatment with miri (NCT02891226).

Aims & Methods: Entry criteria for enrollment included an average daily stool frequency (SF; ≥ 4) and/or the average daily occurrence of abdominal pain (AP; ≥ 2) from the Crohn's Disease Activity Index (CDAI), and a Simple Endoscopic Score for CD ≥ 7 in patients with ileal-colonic or ≥ 4 in patients with isolated ileal disease. Patients were randomised 2:1:1:2 to receive intravenous miri (200 mg, 600 mg, or 1,000 mg) or placebo at weeks 0, 4, and 8. Endpoints in this analysis included changes from baseline in CDAI, SF, and AP at weeks 4, 8, and 12. A mixed effects model for repeated measures analysis was conducted to compare mean changes from baseline across treatment groups for the all-patient cohort and for the biologic-experienced sub-group. Factors in the analysis included treatment, geographic region, baseline score, prior biologic CD therapy (all-patient cohort), visit, and treatment by visit interaction as fixed effects. An unstructured variance covariance was used.

Results: A total of 191 patients were randomised at baseline, which included biologic naïve (n=71) and biologic-experienced patients (n=120). Changes in CDAI, SF, AP at weeks 4, 8 and 12 compared to baseline are shown in the Table. In the all-patient cohort, statistically significant improvement in CDAI was observed with miri 600 mg and in SF with miri 200 mg compared to placebo as early as week 4 (Table). Improvement in CDAI and SF occurred with all miri doses (200 mg, 600 mg, 1,000 mg) at weeks 8 and 12 and in AP at weeks 8 and 12 with all miri doses. Compared to placebo, the subgroup of biologic-experienced patients showed statistically sig-

nificant improvement in CDAI at week 4 (miri 600 mg) and at weeks 8 and 12 with all three doses. Further, significant improvement was observed in SF at week 12 (miri 600 mg and miri 1,000 mg) and in AP at week 8 (miri 600 mg) and week 12 (miri 600 mg and miri 1,000 mg).

Conclusion: Treatment with miri induced early improvement in clinical symptoms and disease activity in patients with moderately-to-severely active CD.

	Crohn's Disease Activity Index Change from BL (LSM)	Stool Frequency Change from BL (LSM)	Abdominal Pain Change from BL (LSM)							
All patients N=191* (Bio-exp N=120)**	Wk 4	Wk 8	Wk 12	Wk 4	Wk 8	Wk 12	Wk 4	Wk 8	Wk 12	
Placebo	-38.5 [-41.8]	-39.2 [-30.8]	-35.2 [-30.7]	-1.1 [-1.3]	-1.2 [-1.2]	-1.3 [-1.4]	-0.3 [-0.4]	-0.3 [-0.4]	-0.3 [-0.4]	
Miri 200mg	-69.8 [-48.3]	-94.5\$ [-74.4†]	-106.5\$\$ [-81.9†]	-2.4‡ [-2.0]	-2.7\$ [-2.2]	-2.9\$ [-2.0]	-0.4 [-0.2]	-0.6† [-0.4]	-0.7‡ [-0.4]	
Miri 600mg	-81.1‡ [-82.6†]	-129.8\$\$ [-131.8\$\$]	-139.8\$\$ [-142.3\$\$]	-1.7 [-1.2]	-2.7\$ [-2.5]	-3.0\$ [-2.8†]	-0.5 [-0.5]	-0.9\$ [1.0\$]	-0.8\$ [-0.9\$]	
Miri 1000mg	-54.1 [-61.8]	-85.5\$ [-85.3‡]	-107.0\$ [-103.8\$]	-1.5 [-1.6]	-2.2‡ [-2.1]	-2.9\$ [-2.9\$]	-0.4 [-0.4]	-0.6‡ [-0.6]	-0.7\$ [-0.6†]	

†p<0.1, ‡p<.05, \$p<0.01; \$\$p<0.001 for miri versus Placebo

*Sample size of treatment groups from all patients: Placebo (n=64), Miri 200 mg (n=31), Miri 600 mg (n=32), Miri 1,000 mg (n=64). **Sample size of treatment groups from biologic-experienced patients: Placebo (n=43), Miri 200 mg (n=19), Miri 600 mg (n=19), Miri 1,000 mg (n=39).

Baseline values for CDAI in the Placebo, Miri 200mg, Miri 600mg, and Miri 1000mg groups, respectively: 304.7, 348.3, 298.1, 304.5 (all patients); 287.2, 343.3, 299.3, 307.3 (Bio-exp)

Baseline values for Stool Frequency in the Placebo, Miri 200mg, Miri 600mg, and Miri 1000mg groups, respectively: 6.4, 7.4, 6.4, 6.6 (all patients); 6.1, 7.8, 6.6, 6.6 (Bio-exp)

Baseline values for Abdominal Pain in the Placebo, Miri 200mg, Miri 600mg, and Miri 1000mg groups, respectively: 1.9, 2.0, 1.7, 1.9 (all patients); 1.8, 2.0, 1.7, 1.8 (Bio-exp)

Abbreviations: BL, baseline; LSM, least square means; Miri, mirikizumab;

Wk, Week; Bio-exp, biologic experienced patients

[Treatment Effect of Mirikizumab vs. Placebo in Reducing Crohn's Disease Activity Index, Stool Frequency, and Abdominal Pain Over Time]

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P0591

IMMUNOSUPPRESSANT MAINTENANCE THERAPY IN INFLAMMATORY BOWEL DISEASE: A REVIEW OF SERIOUS ADVERSE EVENTS

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Introduction: The pathogenesis of Inflammatory Bowel Disease (IBD) is multifactorial, and targeted treatment is not yet available. Instead, medical therapies that suppress various immunological pathways involved in inflammation are used in the maintenance treatment of IBD. Adverse events, including serious infection and cancer, have been associated with such treatments. To enable informed treatment decisions, these risks need to be understood in greater detail.

Aims & Methods: To systematically review the literature to provide a comprehensive overview of the risk of serious adverse events associated with immunosuppressive maintenance therapies in IBD. This review assessed the risk of malignancy or serious infection with maintenance treatments in IBD and was conducted according to PRISMA guidelines. Searches of MEDLINE and EMBASE were performed from 2000 up to March 2020 using three key search themes: immunosuppression, IBD and adverse events.

Results: A total of 1610 citations were retrieved with 45 studies deemed suitable for inclusion.

Thiopurines were associated with an increase in the risk of cancer overall as well as an increase in the risk of lymphoma and non-melanoma skin cancer (NMSC). Thiopurine use was also associated with an increase in the risk of serious infection, especially of viral aetiology (HR=9.01; 95% CI: 6.61-12.3) compared to bacterial infection (HR=1.89; 95% CI: 1.09-3.27) (1).

Anti-TNF agents were not associated with an increase in the risk of overall cancer or NMSC but were found to increase the risk of melanoma skin cancer (MSC) by as much as 88% (OR = 1.88; 95% CI: 1.08-3.29)(2). We cannot confidently exclude the possibility that anti-TNF treatment increases the risk of lymphoma given the findings of a recent, well-powered, nationwide study (HR= 2.41; 95% CI: 1.60-3.64)(3).

An increased risk of serious infection was also seen with anti-TNF therapy (HR=1.71; 95% CI: 1.56-1.88)(1). Relative to thiopurine monotherapy, anti-TNF use was especially associated with bacterial infections (HR=1.71), as opposed to viral infections (HR=0.57)(1).

Moreover, combination therapy, defined as the concomitant administration of thiopurine and anti-TNF agents, increased the risk of overall cancer, lymphoma, NMSC and serious infection. In particular, the risk of lymphoma with combination treatment was found to be 135% greater than the risk of lymphoma associated with thiopurines alone (3).

Conclusion: There is a clear association between thiopurine maintenance therapy and an increased risk of overall malignancy and, in particular, lymphoma and non-melanoma skin cancer (NMSC). Additionally, IBD patients treated with thiopurines are more susceptible to serious infection, especially infections of viral aetiology.

The use of anti-TNF therapy was associated with an increase in the risk of MSC but not overall cancer or NMSC. At the same time, further evidence is required to assess a possible association between anti-TNF treatment and lymphoma.

Combination therapy was found to increase the risk of all adverse events studied, relative to monotherapy with either thiopurines or anti-TNF agents.

This review also highlights the ongoing paucity of data concerning adverse events with the newer biological immunosuppressants in IBD treatment such as vedolizumab and ustekinumab.

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P0592

ABSENCE OF BOWEL URGENCY IS ASSOCIATED WITH IMPROVEMENTS IN CLINICAL OUTCOMES INPATIENTS WITH ULCERATIVE COLITIS RECEIVING MIRIKIZUMAB

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Introduction: Bowel urgency is one of the most common yet often overlooked symptoms experienced by patients with UC¹. Mirikizumab (miri), a humanized monoclonal antibody directed against the p19 subunit of IL-23, demonstrated efficacy², was well-tolerated, and significantly reduced urgency³ in a phase 2 randomized clinical trial in patients with ulcerative colitis (UC). Here we show the relationship between patient-reported urgency and improvements in measures of clinical efficacy.

Aims & Methods: Patients (N=249) were randomized 1:1:1:1 to receive intravenous placebo, miri 50mg or 200mg with possibility of exposure-based dose increases, or fixed miri 600mg every 4 weeks. Patients who achieved clinical response (n=106) at Week 12 were re-randomized 1:1 to double-blind maintenance treatment with miri 200mg subcutaneously

every 4 or 12 weeks and treated through Week 52. Analyses of the association between urgency and clinical efficacy at Weeks 12 and 52 were conducted by pooling treatment arms in the induction and maintenance periods, respectively. Absence of urgency was defined as reporting no urgency for the three consecutive days prior to each scheduled visit, regardless of urgency status at BL. Patients with missing urgency data were imputed as having experienced urgency at that visit. Clinical efficacy in patients with presence or absence of urgency was compared using logistic regression models adjusting for geographic region, prior biologic experience, age, and sex.

Results: As previously reported, miri significantly reduced urgency over 52 weeks of treatment³. At Week 12 and Week 52, patients with absence of urgency had significantly higher rates of improvement on all clinical outcomes examined (clinical remission, clinical response, stool frequency (SF) remission, rectal bleeding (RB) remission, endoscopic remission, histologic remission, mucosal healing; see table for definitions and p values) compared to those with presence of urgency.

Conclusion: Absence of urgency is strongly associated with improved clinical, endoscopic and histologic outcomes. These findings suggest that urgency may be a useful surrogate marker of disease activity and is a distinct symptom that is important to discuss with patients with UC.

	Week 12	Week 52						
All values n (%)	Bowel Urgency Absent (N=91)	Bowel Urgency Present (N=158)	P- value ^a	Adjusted odds ratio (95%CI)	Bowel Urgency Absent (N=66)	Bowel Urgency Present (N=40)	P- value ^a	Adjusted odds ratio (95%CI)
Clinical remission ^b	43 (47.3)	26 (16.5)	0.0019	3.6 (1.6, 8.0)	35 (53.0)	5 (12.5)	<.0001	10.7 (3.3, 35.0)
Clinical response ^c	64 (70.3)	42 (26.6)	<0.0001	6.3 (3.4, 11.6)	62 (93.9)	19 (47.5)	<.0001	24.0 (6.2, 92.5)
Stool frequency remission ^d	63 (69.2)	48 (30.4)	<0.0001	4.8 (2.7, 8.7)	61 (92.4)	16 (40.0)	<.0001	23.3 (6.5, 84.2)
Rectal bleeding remission ^e	74 (81.3)	57 (36.1)	<0.0001	7.2 (3.8, 13.7)	59 (89.4)	22 (55.0)	0.0004	6.6 (2.3, 18.6)
Endoscopic remission ^f	29 (31.9)	17 (10.8)	0.0004	3.6 (1.8, 7.2)	40 (60.6)	11 (27.5)	0.0005	5.6 (2.1, 14.7)
Histologic remission ^g	43 (47.3)	26 (16.5)	<0.0001	4.6 (2.4, 8.0)	40 (60.6)	14 (35.0)	0.0065	3.4 (1.4, 8.3)
Mucosal healing ^h	22 (24.2)	9 (5.7)	0.0003	4.9 (2.1, 11.6)	28 (42.4)	8 (20.0)	0.0113	3.7 (1.3, 10.1)

^aFrom logistic regression model for remissions or responses, adjusted by urgency remission status, age, sex, geographic region and prior biologic experience. Missing values for the clinical outcome and absence of urgency were imputed using non-responder imputation; ^bClinical remission: RB Mayo subscore of 0, SF Mayo subscore of 0 or 1 with a ≥ 1 point decrease from baseline, and Mayo endoscopic subscore of 0 or 1; ^cClinical response: a decrease in the 9-point Mayo subscores (comprising the subscores of rectal bleeding, stool frequency and the endoscopic findings) inclusive of ≥ 2 points and $\geq 35\%$ from baseline with either a decrease of rectal bleeding subscore of ≥ 1 or rectal bleeding subscore of 0 or 1; ^dStool frequency remission: Mayo SF = 0, or 1 with a ≥ 1 point decrease from baseline; ^eRectal bleeding remission: Mayo RB = 0; ^fEndoscopic remission: Mayo endoscopy = 0 or 1; ^gHistologic remission: Geboes grades (2B, 3, 5) are equal to 0; ^hMucosal healing: achievement of both endoscopic remission and histologic remission

[Clinical outcomes of mirikizumab treatment in the absence or presence of bowel urgency]

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P0593

EVALUATION OF CLINICAL RELATIONSHIP BETWEEN FECAL CALPROTECTIN AND ENDOSCOPIC FINDINGS IN ULCERATIVE COLITIS PATIENTS TREATED WITH INFLIXIMAB (CT-P13) SUBCUTANEOUS AND INTRAVENOUS THERAPY: RESULTS FROM A MULTICENTER, RANDOMIZED, CONTROLLED PIVOTAL TRIAL

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Introduction: Fecal calprotectin (FC) is often used to monitor disease activity of ulcerative colitis (UC), but there are still limited data from controlled trials on the correlation of FC levels with degrees of mucosal recovery and on the optimal threshold indicating mucosal healing (MH). The purpose of this study is to investigate the accuracy of FC in monitoring mucosal change in a controlled trial with infliximab CT-P13 subcutaneous (SC) and intravenous (IV) formulations for patients with moderate to severe UC.

Aims & Methods: This is an analysis of a clinical trial which randomized patients with moderately to severely active UC to receive either CT-P13 SC 120/240 mg or IV 5 mg/kg from Week 6 onward, after two infusions of the CT-P13 IV at Weeks 0 and 2. FC levels were assessed at baseline and Week 22. Enzyme-linked immunosorbent assay (Bühlmann Laboratories AG) was used to assess FC concentration. Mucosal healing was defined as Mayo endoscopic subscore (MES) of 0 or 1 via proctosigmoidoscopy and was assessed at baseline and Week 22. Correlation between FC levels and MES as well as correlations of C-reactive protein (CRP), white blood cells (WBC), hemoglobin (Hb), platelet, and albumin with MES at Week 22 were assessed by Spearman's correlation. Wilcoxon test was applied to compare FC levels between patients with and without MH. Additionally, receiver operating characteristic (ROC) analysis was performed to estimate a cut-off level of FC which would indicate MH.

Results: A total of 68 UC patients was included in this analysis; SC arm (n = 33) and IV arm (n = 35). At baseline, median FC level in the entire cohort was 880 µg/g (786 µg/g and 978 µg/g in SC and IV arms, respectively) and proportion of patients with FC level > 250 µg/g was 86.8% (59/68) (87.9% [29/33] and 85.7% [30/35] in SC and IV arms, respectively). The proportion of patients with FC level > 250 µg/g decreased to 39.0% (23/59) at Week 22 (44.4% [12/27] and 34.4% [11/32] in SC and IV arms, respectively). The correlation of MES with FC levels (r = 0.602, p < 0.0001) was numerically better compared to correlations of MES with CRP (r = 0.465, p = 0.0003), WBC (r = 0.252, p = 0.0606), Hb (r = -0.175, p = 0.1978), platelet (r = 0.190, p = 0.1602), and albumin (r = -0.523, p < 0.0001) at Week 22. When the patients were classified into those who achieved MH versus those who did not, FC levels were significantly lower in patients with MH at Week 22 (median [min, max] = 56.0 [10, 1571] µg/g versus 1239.0 [62, 7307] µg/g respectively, p < 0.0001). ROC analysis showed that FC level of 82 µg/g was the

optimal cut-off value that differentiates patients who achieved MH from those who did not with an area under the curve of 0.895, 67.7% sensitivity, and 94.7% specificity (positive predictive value 95.5%, negative predictive value 64.3%).

Conclusion: This analysis of a controlled CT-P13 SC/IV clinical trial showed that FC levels are clearly associated with changes in status of mucosal inflammation, and specifically with improved endoscopic activity in UC patients. These findings support FC as a noninvasive biomarker alternative to endoscopy for monitoring the mucosal response to infliximab (CT-P13) treatment in patients with UC.

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P0594 WITHDRAWN

P0595

CROHN'S DISEASE EXCLUSION DIET INDUCES REMISSION IN ADULTS WITH MILD TO MODERATE CROHN'S DISEASE: PRELIMINARY REPORT FROM A RANDOMISED CONTROLLED TRIAL (CDED-AD TRIAL)

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Introduction: Crohn's disease (CD) exclusion diet (CDED) is a whole-food diet designed to reduce exposure to dietary components that have adverse effects on the microbiome and intestinal barrier. CDED coupled with partial enteral nutrition (PEN) was demonstrated to be effective for induction of remission and reduction in inflammation by week 6 in children with mild - moderate CD.

The role of PEN in induction of remission is unclear. In this study we aimed to evaluate the efficacy of CDED with or without partial enteral nutrition (PEN) in 1.) inducing remission 2.) maintaining remission and 3.) achieving mucosal healing in adults with active mild-moderate CD. Here we report data regarding induction of remission using CDED with PEN or CDED alone at week 6.

Aims & Methods: This is an open label prospective randomized controlled pilot trial assessing the impact of dietary intervention in adults (18 >years) with mild-moderate uncomplicated CD of the terminal ileum and or cecum (up to 5 years from diagnosis) upon remission and mucosal healing. Patients could be included if Harvey Bradshaw Index (HBI) was 5-15, and active disease was demonstrated by colonoscopy or if MR/CT enterography or capsule endoscopy demonstrated active disease in the ileum in addition to elevated calprotectin >200 within the previous 8 weeks of enrollment. Patients were randomized into two arms for a period of 24-weeks: group 1-CDED with Modulen 1000 ml (CDED+PEN) or group 2-CDED alone for the first 6 weeks.

Results: Overall 39/41 patients with 6 weeks follow up (mean age 32.5±11 years, 56% females) were analyzed for remission at week 6: 15 patients - group 1 (CDED+PEN), 24 patients group 2 (CDED alone). Mean HBI for the entire population decreased from 7.3±1.9 at baseline to 3.7±2.7 at week 6 (p=0.001). Response for patients in group 1 and 2 was 11/15 (73.3%) and 15/24 (62.5%) respectively, p=0.48. In group 1, ITT steroid free remission was achieved in 60% (9/15), while 58.3% (14/24) achieved remission in group 2, p=0.91. Mean HBI declined in group 1 from 8.2±2.2 at baseline to 3.4±1.9 at week 6, p=0.01, while in group 2 HBI declined from 6.7±1.6 to 3.9±3.2, p=0.01. Among patients with elevated CRP at baseline median CRP declined in group 1 from 20.1mg/L [IQR 8.6-38] at baseline to 11.8mg/L [IQR 5.5-23], p=0.035 and in group 2 from 14.7 [IQR 8.7-52] to 9 [IQR 5.3-33.9], p=0.045. Among patients in group 1 there were 4 patients who stopped Modulen between week 1 to 3, 3 out of 4 achieved remission using the CDED alone. Among patients in group 2 (CDED alone), 2 patients had Modulen added for nutritional reasons between weeks 1-3, one patient was already in remission prior to adding Modulen.

Conclusion: In this first trial to evaluate CDED prospectively in adults, both CDED with PEN and CDED alone appear to have similar beneficial effects for induction of remission and decline in CRP by week 6. Though the

data for maintenance of remission and mucosal healing from the trial are not yet available, our data suggest that CDED can be used either way for induction of remission in adults with mild to moderate CD.

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P0596

THE PRESENCE OF CITRATE IN ADALIMUMAB-BASED TREATMENTS CORRELATES WITH THE PERCEPTION OF PAIN AFTER SUBCUTANEOUS INJECTION, IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Inflammatory bowel disease (IBD) includes Ulcerative colitis and Crohn disease, two chronic and debilitating conditions of the digestive tract. Currently there is no cure, but different medications are available to maintain disease remission. Among them, the human anti-TNF monoclonal antibody adalimumab (ADA), is widely used in IBD patients. Its formulation greatly improved with the removal of the citrate buffer - which is known to cause pain immediately after the subcutaneous injection¹. Despite the evidence that correlates the presence of citrate and the perception of pain in IBD patients², and the fact that biosimilars without citrate are available in the Spanish market, the commercialization of biosimilars with citrate was approved and are now used in different hospitals. **Aims & Methods:** This study aims to show that Spanish IBD patients under ADA treatment are sensible to the presence of citrate in the drug formulation and that this correlates with the perception of pain immediately after subcutaneous injection as well as to treatment satisfaction.

The information was anonymously provided IBD patients by completing an online survey that was freely accessible in the ACCU España website, Facebook and Instagram pages.

Patients were asked to 1) indicate which treatment they were using, 2) tell if the injection was painful, 3) quantify the pain (from 0= no pain, to 10 = extreme pain) and 4) to specify treatment satisfaction.

Results: A total of 360 patients completed the questionnaire. The percentage of patients who claim to feel pain after injecting the drug is lower in these groups compared to the group of patients using medications with citrate. Additionally, the score of pain intensity reported by patients is more elevated after the injection of drugs containing citrate, being 1.8 and 1.5 times higher than the citrate-free original adalimumab and -biosimilars, respectively (Table 1).

Conclusion: IBD patients must follow long-life treatments in order to maintain disease remission and have a greater quality of life. Adherence to treatment is fundamental to minimize the comparison of unpredictable flares or complications. Our preliminary results show that the presence of citrate and not the type of drug (original or biosimilar) correlates with the perception of pain in IBD patients and as well as to treatment satisfaction. Solutions should be found in order to avoid the distribution and administration of drugs that are considered painful by patients, when better tolerated alternatives are available in the market.

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P0597

EXCLUSIVE ENTERAL NUTRITION OR PREDNISOLONE INDUCTION TREATMENT: CLINICAL AND ENDOSCOPIC EVALUATION OF NEW-ONSET LUMINAL PAEDIATRIC CROHN'S DISEASE

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Introduction: To induce remission in luminal paediatric Crohn's Disease (CD) the European guideline recommends treatment with exclusive enteral nutrition (EEN) or oral prednisolone. To maintain remission azathioprine (AZA) usually is started. We hypothesize in moderate-to-severe paediatric CD patients induction by EEN or prednisolone followed by AZA maintenance insufficiently provides disease control.

Aims & Methods: To thoroughly evaluate whether EEN and prednisolone induce remission which consequently is maintained by AZA in newly diagnosed moderate-to-severe paediatric CD patients.

This is a secondary analysis of prospectively collected data from the "TISKIDS" randomised control trial. Patients assigned to the conventional step-up treatment arm were included. Patients were aged 3-17 years and had new-onset, untreated luminal CD with weighted paediatric CD activity index (wPCDAI) >40. Induction treatment consisted of EEN (polymeric feeding for 6-8 weeks after which normal diet was gradually reintroduced within 2-3 weeks) or oral prednisolone (1 mg/kg daily with a maximum of 40 mg for 4 weeks, followed by tapering down 5 mg per week until stop); all received AZA as maintenance treatment introduced from start. Patients with loss of response during AZA monotherapy stepped up to infliximab therapy after checking AZA metabolites and optimizing its dosing in case of suboptimal levels. Ten weeks after treatment initiation, rates of clinical remission (wPCDAI < 12.5), mucosal healing by endoscopy (SES-CD < 3) and fecal calprotectin levels (< 250 ug/g) were assessed. Linear growth was assessed at 52 weeks after treatment initiation.

Results: 27/47 patients received EEN and 20/47 prednisolone. At baseline there were no significant differences within the two groups. At 6 weeks, 11/23 patients (48%) treated with EEN were in clinical remission, compared to 10/18 patients (56%) patients treated with prednisolone (p=0.556). At 10 weeks, 9/26 patients (35%) treated with EEN and 8/20 (40%) patients treated with prednisolone (p=0.708) were in clinical remis-

sion. At 10 weeks 29/47 (62%) consented to endoscopy. Mucosal healing rates were 3/16 (19%) in EEN treated patients (median SES-CD 10 [IQR 3.3-17.5]) and 1/13 (8%) in prednisolone treated patients (median SES-CD 6 [IQR 3.5-17.5]) ($p=0.948$). Likewise, only a minority of patients had faecal calprotectin levels below 250 $\mu\text{g/g}$ (EEN: 4/21 (19%) vs. prednisolone: 4/16 (25%) $p=0.663$). Step-up to infliximab was necessary in 16/27 (59%) patients treated with EEN and 13/20 (65%) with prednisolone, respectively. At one year after start of therapy, the SDS height for age deteriorated in 19/27 (70%) of the EEN-treated patients and in 10/19 (53%) of the prednisolone-treated patients ($p=0.22$).

Conclusion: In children with newly diagnosed moderate-to-severe CD, both EEN and prednisolone insufficiently induced remission. Ten weeks after either EEN or prednisolone treatment to induce remission, mucosal healing rates were low. After one year, in the majority of patient's growth retardation had increased. No difference was found between the treatment groups. Insufficient remission induction may explain why AZA maintenance treatment was inadequate and the majority of patients needed treatment intensification to infliximab. Another explanation for these findings is that in our study normal diet was re-introduced 2-4 weeks before endoscopic assessment. Maybe mucosal healing was attained by EEN but did not sustain after re-introduction of normal diet, despite AZA maintenance treatment.

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P0598

RAC1/PSTAT3 EXPRESSION IN LYMPHOCYTES MAY SERVE AS A PHARMACODYNAMIC MARKER TO OPTIMIZE PERSONALIZED THIOPURINE THERAPY IN IBD PATIENTS

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Introduction: Thiopurine derivatives, such as azathioprine (AZA) and mercaptopurine (MP), still remain standard treatment of Inflammatory Bowel Diseases (IBD). To optimize thiopurine therapy, genotyping of the enzyme

thiopurine S-methyltransferase (TPMT), and pharmacokinetic-based therapeutic drug monitoring are commonly applied. However, pharmacokinetic information is of limited use to predict clinical effectiveness. A direct pharmacodynamic marker in lymphocytes may be more useful to predict therapeutic outcome of thiopurine therapy. The immunosuppressive mechanism of thiopurines is principally based on inhibition of the Ras-related C3 tubulin toxin substrate 1 (Rac1) by the active thiopurine metabolite 6-thioguanine triphosphate causing T-cell apoptosis by the downstream transcription factor signal transducer and activator of transcription 3 (STAT3). We performed a series of experiments to assess feasibility of measurement of Rac1 and activated STAT3 (pSTAT3) in blood derived leukocytes of IBD-patients with variable immunosuppressive therapies and compared it with healthy controls.

Aims & Methods: The aim of this study is to explore whether expression of Rac1 and pSTAT3 in lymphocytes may be used as a potential pharmacodynamic marker to optimize personalized thiopurine therapy in IBD patients. We performed a single centre pilot study in 3 parallel groups to assess feasibility. Per group six patients were included so far:

- 1) IBD patients with active disease without systemic immunomodulating therapy,
- 2) IBD patients on AZA or MP monotherapy, and
- 3) healthy controls.

Results: Compared to healthy controls (1.01 Arbitrary Units (AU), range 0.67 - 1.29), Rac1 expression in lymphocytes was increased in IBD-patients using thiopurine therapy (1.30 AU, range 1.07 - 2.07). This upregulation was not found in therapy-naïve IBD patients (1.00 AU, range 0.60 - 1.98). An increase in absolute pSTAT3 expression compared to healthy controls (0.67 AU, range 0.58 - 2.89) was found in both therapy-naïve IBD patients (2.40 AU, range 0.64 - 3.37) and patients on thiopurine therapy (2.09 AU, range 1.68 - 2.40). Furthermore, pSTAT3 expression corrected for Rac1 expression was decreased in IBD patients treated with thiopurines (1.34 AU, range 1.10 - 2.20) compared to therapy-naïve IBD patients (2.93 AU, range 0.60 - 4.23). Notably, Rac1 corrected pSTAT3 expression in the latter patient group showed a greater interindividual variability compared to the other groups.

Conclusion: Expression of Rac1 and pSTAT3 in lymphocytes differed between therapy-naïve IBD patients, IBD patients on thiopurine therapy and healthy controls. We theorized that upregulation of Rac1 expression may be an effect of cell adaptation to effective inhibition of the Rac1/pSTAT3 cascade. Although the absolute expression of the activated downstream transcription factor STAT3 was comparable between IBD patients with or without thiopurine therapy, Rac1-corrected pSTAT3 expression was decreased in IBD patients on thiopurine therapy. Further test characteristics, statistical analysis, particularly sensitivity and specificity, have yet to be determined.

In conclusion, Rac1 expression in combination with pSTAT3 expression may serve as a potential pharmacodynamic marker for thiopurine therapy.

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P0599

HIGHER VS STANDARD ADALIMUMAB INDUCTION AND MAINTENANCE TREATMENT IN PATIENTS WITH MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS: INTEGRATED RESULTS FROM THE PHASE 3 SERENE-UC STUDY

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Introduction: SERENE-UC (NCT02065622) was a Phase 3 study of higher vs standard adalimumab dosing regimens for induction (HIR vs SIR) and maintenance therapy in patients (pts) with moderately-to-severely active ulcerative colitis. Data from the Main (excluding Japan) study have been reported; here we report data on the integrated (Main + Japan) population.

Aims & Methods: Pts were randomized to adalimumab HIR (160mg/week [Wk] at Wk0-3, 40mg at Wk4 and Wk6) or SIR (160mg at Wk0, 80mg at Wk2, 40mg at Wk4 and Wk6) for 8 weeks induction. Pts completing induction were re-randomized to adalimumab 40mg every week (40EW) or 40mg every other week (40EOW) for 44 weeks maintenance. Primary endpoint (EP) of the induction study was the proportion of patients achieving clinical remission (CR; Full Mayo score [FMS] ≤2, no subscore >1) at Wk8. Primary EP of the maintenance study was the proportion of Wk8 responders (decrease in FMS ≥3 and ≥30% from baseline [BL] and decrease in rectal bleeding subscore [RBS] ≥1 or absolute RBS ≤1) achieving CR at Wk52. Safety was assessed throughout.

Results: 952 pts enrolled. At Wk8, rates of CR (13.8% vs 11.6%) and discontinuation (DC, 10.1% vs 12.4%) were similar between HIR and SIR groups; proportions of patients meeting ranked secondary EPs are shown in the Table. 846 pts, including 412 Wk8 responders, completed induction and were re-randomized to maintenance therapy. At Wk52, significantly more Wk8 responders achieved CR with 40EW vs 40EOW (41.1% vs 30.1%; p=0.045). During maintenance, the DC rate was numerically lower with 40EW vs 40EOW (18.3% vs 27.6%). Key ranked secondary EPs were numerically higher with 40EW vs 40EOW (Table), as were other ranked secondary

EPs, n/N (%) [nominal p-value]: Wk8 remitters achieving CR, 29/52 (55.8) vs 20/45 (44.4) [0.312]; Wk8 remitters achieving endoscopic improvement, 32/52 (61.5) vs 25/45 (55.6) [0.600]; Wk8 remitters taking steroids at BL who are steroid free for ≥90 days, 25/35 (71.4) vs 18/32 (56.3) [0.210]; Wk8 remitters taking steroids at BL who are steroid free for ≥90 days and in CR, 18/35 (51.4) vs 12/32 (37.5) [0.299]; Wk8 responders with inflammatory bowel disease questionnaire (IBDQ) response, 115/175 (65.7) vs 102/163 (62.6) [0.513]; Wk8 nonresponders with CR, 28/175 (16.0) vs 22/182 (12.1) [0.292]; Wk8 nonremitters with CR, 71/298 (23.8) vs 51/300 (17.0) [0.046]; Week 8 responders achieving endoscopic subscore =0, 62/175 (35.4) vs 44/163 (27.0) [0.109]; Wk8 remitters achieving endoscopic subscore =0, 23/52 (44.2) vs 19/45 (42.2) [0.901]; Wk8 responders with response in IBDQ, bowel symptom domain, 125/175 (71.4) vs 102/163 (62.6) [0.076]; Wk8 responders with response in IBDQ fatigue item, 104/175 (59.4) vs 90/163 (55.2) [0.440]. Higher dosing regimens were generally well tolerated.

Conclusion: The integrated population of SERENE-UC demonstrated numerically greater efficacy for HIR vs SIR, consistent with the Japan-only population. At Wk52, CR among Wk8 responders was significantly higher with adalimumab 40EW vs 40EOW. All dosing regimens were well tolerated.

Ranked secondary endpoints, Induction study	Adalimumab higher induction regimen (N=573), n (%)	Adalimumab standard induction regimen (N=379), n (%)	Nominal p-value
Endoscopic improvement (endoscopic subscore of 0 or 1)	175 (30.5)	102 (26.9)	0.203
Fecal calprotectin <150mg/kg	129 (22.5)	74 (19.5)	0.240
Inflammatory bowel disease questionnaire response (increase of inflammatory bowel disease questionnaire ≥16 from baseline)	372 (64.9)	230 (60.7)	0.159
Clinical response (per Full Mayo score)	271 (47.3)	147 (38.8)	0.008
Endoscopic remission (endoscopic subscore of 0)	74 (12.9)	38 (10.0)	0.168
Key ranked secondary endpoints, Maintenance study	Adalimumab 40mg every week, n/N (%)	Adalimumab 40mg every other week, n/N (%)	Nominal p-value
Week 8 responders achieving endoscopic improvement (endoscopic subscore of 0 or 1)	91/175 (52.0)	68/163 (41.7)	0.066
Week 8 responders taking steroids at baseline who are steroid free for ≥90 days	80/108 (74.1)	56/103 (54.4)	0.003
Week 8 responders taking steroid at baseline who are steroid free for ≥90 days and in clinical remission	43/108 (39.8)	29/103 (28.2)	0.088

[Ranked secondary endpoints for induction and maintenance dosing regimens]

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P0600

THE REAL-WORLD EFFICACY AND SAFETY OF VEDOLIZUMAB IN BIO-NAÏVE PATIENTS WITH INFLAMMATORY BOWEL DISEASE - AN INTERIM ANALYSIS FROM A DANISH NATIONAL COHORT STUDY

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Introduction: The effectiveness of vedolizumab (VDZ), a humanized monoclonal anti- $\alpha 4\beta 7$ integrin antibody, has been shown to be decreased by prior exposure to biologic therapies but only few studies have examined the efficacy of VDZ as a first line biologic therapy (FLBT) in a real-world setting.

Aims & Methods: We aimed to conduct a national retrospective cohort study investigating the real-world clinical effectiveness and safety of VDZ in bio-naïve patients with Crohn's disease (CD) and ulcerative colitis (UC) in Denmark treated between November 2014 and November 2019. The primary outcomes included clinical remission defined as Harvey Bradshaw Index ≤ 4 or Simple Clinical Colitis Activity Index ≤ 2 , biochemical remission defined as C-reactive protein (CRP) < 5 or f-calprotectin (FC) < 200 and endoscopic remission defined as Mayo Endoscopic Subscore ≤ 1 . The outcomes were assessed at initiation of VDZ (baseline), at week 6 (W6), week 14 (W14) and week 30 (W30). Data from follow-up were compared to baseline data as univariate comparisons through Wilcoxon Signed-Rank test and Fisher's exact test for continuous and categorical variables, respectively. A p-value < 0.05 was considered significant.

Results: A total of 40 patients from 15 sites in Denmark received VDZ as FLBT of which baseline data of 18 patients (UC: 10, CD: 8) were available and included in this interim analysis. The most frequent reasons for receiving VDZ as FLBT were co-occurring or prior malignancy (9), a combination of older age and infectious or cardiovascular comorbidities (5) or multiple sclerosis (3). At baseline, 9 (50%) patients received concomitant systemic steroids, while two patients received azathioprine and mercaptopurine. Only one patient received an intestinal resection prior to initiation of VDZ.

We observed a rapid induction of remission at week 6 among 44% of our cohort while every third patient achieved steroid-free clinical (SFC) remission. As shown in Table 1, the proportion of patients achieving clinical, biochemical and SFC remission increased significantly during follow-ups and at week 30, 50% of the patients were in SFC remission ($p < 0.01$).

	Week 0 Baseline data available for 18 patients	Week 6	p-value (baseline vs W6)	Week 14	p-value (baseline vs W14)	Week 30	p-value (baseline vs W30)
Clinical response (N (%))		9/18 (50)		11/16 (69)		9/16 (56)	
Clinical remission (N (%))	4/18 (22)	8/18 (44)	0,3	11/16 (69)	0,01	8/16 (50)	0,15
Steroid free clinical remission (N (%))	1 (5)	6/18 (33)	0,09	7/16 (44)	0,01	8/16 (50)	<0,01
Biochemical remission (N (%))	4 (22)	5/18 (28)	0,71	11/16 (69)	0,01	10/16 (63)	0,03
Endoscopic remission (N (%))	1 (5)			3/3 (100)			
HBI (median(IQR))	5 (5-10)	3 (2-6)		4 (3-6)		3 (1-3)	
SCCAI (median(IQR))	5 (4-8)	1 (0-1)		1 (0-2)		2 (2-4)	
p-CRP (median(IQR))	7 (4-11)	6 (2-10)	NS	4 (2-12)	0,03	4 (2-15)	0,28
f-calprotectin (median(IQR))	1593 (769-2261)					70 (63-183)	
Cumulated hospitalization rates (N (length in days))	0	1 (2)		1 (2)		0	
Adverse events (N with description)	1 (arthralgia)	2 (nausea and headache)		1 (tingling)		2 (heatness and arthralgia)	

[Table 1: Summary of study results.]

Accordingly, none of the patients required IBD related surgeries. Subgroup analysis on CD and UC showed no difference in proportion of response and remission rates.

During follow-up, only one patient discontinued VDZ therapy due to primary non-response while two patients switched to other biologic therapies to target co-occurring multiple sclerosis. As presented in Table 1, every third patient experienced mild adverse effects to VDZ, but none required discontinuation of VDZ.

Conclusion: These interim data from a national study support short and long-term efficacy of VDZ in bio-naïve patients with CD and UC in a real-world setting.

Disclosure: Nothing to disclose

P0601 WITHDRAWN

P0602 WITHDRAWN

P0603

EFFICACY AND SAFETY OF RE-INDUCTION WITH INTRAVENOUS USTEKINUMAB IN PATIENTS WITH CROHN'S DISEASE AND LOSS OF RESPONSE TO THAT DRUG

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Introduction: A relevant percentage of patients treated with ustekinumab (UST) may lose response to maintenance treatment (IM-UNITI study). Given the relatively few therapeutic alternatives available in Crohn's disease, measures to restore response in these patients may be of great use in clinical practice. Published data on the efficacy of re-induction with intravenous (IV) UST in patients who lose response are very scarce. Our objective was to evaluate the short-term efficacy and safety of IV UST reinduction in patients with Crohn's disease who, after achieving response to that drug, lose response to this treatment.

Aims & Methods: Retrospective, observational, multicenter study with post-reinfusion evaluation (weeks 8 and 16, or a previous time when due to lack of response it was decided to definitively suspend UST). The Harvey-Bradshaw index was used to evaluate response to reinduction IV with UST. A complete remission was considered a final score ≤ 4 points, and partial response a score >4 but with a 3 point decrease in the index with respect to the baseline situation. Information was also collected on side effects and treatment decisions made after re-induction IV.

Results: Thirty-one patients from 10 centres were included (51.6% male, 35.5% smokers, 48.4% ileal involvement, 45.5% perianal disease). Previous therapies: 29 azathioprine (96.8%); 10 mercaptopurine (32.3%); 19 infliximab (64.5%); 24 adalimumab (80.6%), 12 vedolizumab (40.0%). 48.4% of patients had previous failure to two biologics and 22.6% to three. At entry into the study, 15 patients (48.4%) had UST every 8 weeks, 4 every 6 weeks (12.9%) and 12 every 4 weeks (38.7%). At week 8 after re-induction, 51.6% (N=16) were in remission and 6.4% (N=2) had partial response. At week 16, 41.9% (N=13) were in remission and 6.4% (N=2) had partial response. Mean values of basal calprotectin (microg/g) and C-reactive protein (mg/L) at 8 and 16 weeks were respectively: 1358.1±3038.4; 597.4±970.1; 211.8±167.0 and 11.6±13.3; 9.7±19.7; 7.3±7.8 (p>0.05). Patients who achieved remission at week 16 had lower C-reactive protein levels than those who did not respond (3.0±1.7 vs 14.1±9.0 mg/L; p=0.01).

No adverse effects related to re-induction were observed. In patients who failed reinduction, treatment with vedolizumab was initiated in 5, intestinal resection was performed in 2, and a steroid course was prescribed in the rest of subjects.

Conclusion: Intravenous re-induction with UST is an effective and safe measure at least in the short term that achieves recovery of response in approximately half of the patients with refractory Crohn's disease who experience a loss of response to such treatment.

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P0604

VEDOLIZUMAB CLINICAL DECISION SUPPORT TOOL PREDICTS EFFICACY OF VEDOLIZUMAB BUT NOT USTEKINUMAB IN REFRACTORY CROHN'S DISEASE

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Introduction: Vedolizumab clinical decision support tool (VDZ CDST) was recently developed and validated to predict vedolizumab efficacy in patients with Crohn's disease. VDZ CDST includes 5 common predictors: no prior bowel surgery, no prior anti-TNF exposure, no prior fistulizing disease, albumin and CRP. VDZ CDST ≤ 13 points and >19 points predicts respectively a low and a high probability of response to vedolizumab. VDZ CDST items are those of severity of Crohn's disease and there is uncertainty as to whether they are predictive factors of response to vedolizumab or prognostic markers of response to any drug.

Aims & Methods: We aimed to assess the VDZ CDST as a predictive factor of response of vedolizumab and ustekinumab, in patients with Crohn's disease refractory or intolerant to anti-TNF. We included consecutive patients with Crohn's disease refractory or intolerant to at least one anti-TNF and starting either vedolizumab or ustekinumab in five university hospitals of the Paris area, between May 2014 and August 2018. Patients with pouchitis, ostomy and extra-intestinal manifestation, or in whom prevention of post-operative recurrence was the indication for treatment were excluded. The main endpoint was the steroid free-clinical remission at week 48. Difference of steroid free-clinical remission rates in VDZ CDST classes (CDST ≤ 13 , 13<CDST ≤ 19 and CDST >19) were compared by a chi square test for trend. Then, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for a VDZ CDST >13 were specified. Finally, the VDZ CDST area under the receiver operating characteristic curve were computed in each group.

Results: 180 patients were included, 94 received vedolizumab (CDST ≤ 13 : 32, 13<CDST ≤ 19 : 52, CDST >19 : 10) and 86 received ustekinumab (CDST ≤ 13 : 16, 13<CDST ≤ 19 : 60, CDST >19 : 10). At week 48, in the vedolizumab group, steroid-free clinical remission was achieved in 9.4% with a CDST ≤ 13 , 28.8% with a CDST between 13 and 19, and 80.0% with a CDST >19 ($p < 0.0001$). In the ustekinumab cohort steroid-free clinical remission was achieved in 37.5% with a CDST ≤ 13 , 50.0% with a CDST between 13 and 19, and 50.0% with a CDST >19 ($p = 0.46$).

A cutoff-value of 13 points identified patients in steroid-free clinical remission at week 48 with a sensitivity of 0.88 (95%CI: 0.70-0.98), a specificity of 0.43 (95%CI: 0.31-0.55), a PPV of 0.37 (95%CI: 0.25-0.50) and a NPV of 0.91 (95% CI: 0.75-0.98) in the vedolizumab group. In the ustekinumab group,

the sensitivity was 0.85 (95%CI: 0.71-0.94), specificity was 0.22 (95%CI: 0.11-0.37), PPV was 0.50 (CI95%: 0.38-0.62) and NPV was 0.62 (95%CI: 0.35-0.85). CDST identified steroid-free clinical remission with an area under the curve of 0.69 (95%CI: 0.57-0.82) for vedolizumab and 0.52 (95%CI: 0.40-0.65) for ustekinumab.

Conclusion: The previously built VDZ CDST is associated with vedolizumab but not ustekinumab effectiveness in Crohn's disease patients refractory or intolerant to anti-TNF.

Disclosure: HA, JK and AM declare no competing interest. AA received honoraria from Abbvie, Hospira, Takeda, Gilead, Biocodex, Janssen, Tillotts, Ferring and MSD. XT received honoraria from Abbvie, MSD, Takeda, Ferring, Norgine and Janssen. MA received honoraria from Abbvie, MSD, Janssen, Takeda, Pfizer, Novartis, Ferring, Tillotts, Celgene and Genentech/Roche. YB received honoraria from Abbvie, Biogaran, Boehringer Ingelheim, Celgene, Ferring, Gilead, Hospira, Janssen, Mayoly-Spindler, MSD, Norgine, Pfizer, Roche, Samsung Bioepis, Sandoz, Sanofi, Shire, Takeda, UCB. LB received honoraria from Janssen, Pfizer, Allergan, AbbVie, Janssen, MSD, Ferring Pharmaceuticals, Mayoly-Spindler, Takeda and Tillotts, and research support from Abbott, Ferring Pharmaceuticals, Hospira-Pfizer, Janssen, MSD, Takeda and Tillotts. FC received honoraria from Amgen, BMS, Enterome, Ferring, Janssen, Medtronic, Pfizer, Pharmacosmos and Roche as well as lecture fees from Abbvie, Astra, BMS, Ferring, Janssen, MSD, Pfizer, Pileje, Takeda and Tillotts.

P0605

THE REAL-WORLD EFFICACY AND SAFETY OF VEDOLIZUMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES - A DOUBLE-CENTER DANISH EXPERIENCE

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Introduction: Vedolizumab (VDZ) is a humanized monoclonal anti- $\alpha 4\beta 7$ integrin antibody approved for treatment of moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC) since May 2014.

Aims & Methods: We aimed to conduct a double center retrospective cohort study focusing on the clinical effectiveness and safety of VDZ for all patients with CD and UC treated between November 2014 and November 2019 in a real-world Danish setting. The primary outcomes included clinical remission defined as Harvey Bradshaw Index ≤ 4 or Simple Clinical Colitis Activity Index ≤ 2 , biochemical remission defined as C-reactive protein (CRP) < 5 or f-calprotectin (FC) < 200 and endoscopic remission defined as Mayo Endoscopic Subscore ≤ 1 . The outcomes were assessed at initiation of VDZ (baseline), week 14 (W14), week 30 (W30), week 52 (W52) and week 104 (W104). Data from follow-up were compared to baseline data through paired t-tests and differences between CD and UC were explored through Pearson's chi-squared tests.

Results: A total of 190 patients (UC: 97, CD: 85, unclassified: 8) were included in this study. The disease localization and behavior of CD was L1: 22%, L2: 42%, L3: 31%, L4: 8%, B1: 49%, B2: 51%, and disease extent of UC was E1: 12%, E2: 50% and E3: 38% according to the Montreal Classification. The patients were refractory to a median of 2 (IQR 1-2) prior biologic therapies. At baseline, 42% received systemic steroids, 23% received azathioprine and 11% received mercaptopurine. During follow-up, an increased proportion of patients achieved clinical response (W14: 41%, W30: 42%, W52: 38%, W104: 40%), clinical remission (W0: 18%, W14: 40%, W30: 41%,

W52: 38%, W104: 34%) and steroid-free clinical remission (W0: 5%, W14: 33%, W30: 36%, W52: 32% and W104: 34%). As presented in Table 1, we observed biochemical responses and remissions of the same order of magnitude, which were attributed to a reduction of FC rather than CRP. Patients with CD and UC were also analyzed separately but they only differed in a higher proportion of steroid-free clinical remission among patients with UC after 52 weeks of treatment (60% vs 40%, $p=0.03$). In patients discontinuing VDZ, we observed a decrease of IBD-related surgeries from 69% at week 30 to 24% at week 104 ($p<0.01$).

The requirements of hospital admissions were sparse after initiation of VDZ and, accordingly, VDZ was considered safe with an adverse effect rate of 6% at initiation of therapy. One serious adverse event (anaphylactic reaction) was registered to VDZ.

	Week 0 N= 190 patient (Baseline data available for 174 patients)	Week 14 (163 patients)	P- value	Week 30 (137 patients)	P- value	Week 52 (117 patients)	P- value	Week 104 (79 patients)	P- value
Clinical response (N (%))		72 (41)		70 (42)		63 (38)		55 (40)	
Clinical remission (N (%))	31 (18)	71 (40)		68 (41)		62 (38)		47 (34)	
Steroid free clinical remission (N (%))	8 (5)	59 (33)		60 (36)		53 (32)		46 (34)	
Biochemical remission (N (%))	43 (25)	56 (29)		66 (37)		63 (41)		44 (30)	
Endoscopic remission (N (%))	2 (1)	0 (0)		5 (22)		10 (34)		12 (39)	
HBI (median(IQR))	8 (5-11)	6 (3-9)	0,01	5 (2-7)	0,02	5 (2-7)	<0,01	3 (1-6)	0,12
SCCAI (median(IQR))	6 (4-8)	2 (0-6)	<0,01	2 (0-4)	<0,01	2 (0-3)	<0,01	1 (0-3)	<0,01
p-CRP (median(IQR))	4 (2-12)	4 (2-11)	0,8	2 (2-9)	0,95	2 (2-5)	0,01	3 (2-8)	0,66
f-calprotectin (median(IQR))	940 (214-1800)	299 (76-1688)	0,02	95 (36-979)	<0,01	84 (37-467)	<0,01	76 (29-696)	0,01
Cumulated hospitalization rates (median(IQR))	1 (0-2)	1 (0-2)	0,55	1 (0-2)	0,71	1 (0-2)	0,52	1 (0-2)	0,69
Adverse events (N (%))	11 (6)	3 (2)		1 (1)		2 (2)		1 (1)	
Discontinuation due to primary/ secondary non- response (N (%))	14 (7)	15 (8)		14 (8)		9 (5)		15 (10)	
Discontinuation due to achievement of remission (N (%))	1 (0.5)	0		1 (1)		0		5 (6)	
Discontinuation due to adverse effects (N (%))	7 (4)	3 (2)		1 (1)		1 (1)		0	
Requirement of surgery after discontinuation (N (%))	13 (52)	7 (39)		11 (69)		4 (36)		5 (24)	
Requirement of other classes of biologic therapies after discontinuation (N (%))	2 (8)	12 (67)		7 (44)		9 (82)		12 (57)	

[Table 1: Summary of study results.]

Conclusion: These data support short- and long-term effectiveness and safety of VDZ for patients with Crohn's disease and ulcerative colitis in a real-world setting.

Disclosure: Nothing to disclose

P0606

EFFICACY OF USTEKINUMAB FOR ACTIVE PERIANAL FISTULIZING CROHN'S DISEASE: A DOUBLE CENTER COHORT STUDY AND A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE CURRENT LITERATURE

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Introduction: Ustekinumab (UST), a human monoclonal anti-IL12/23p40 antibody, has shown promising efficacy in fistula response and healing among patients with perianal Crohn's disease (pCD) in a post hoc pooled analysis of data from the CERTIFI, UNITI-1 and UNITI-2 trials. However, the efficacy has only been investigated in few studies.

Aims & Methods: We aimed to conduct a double center retrospective cohort study focusing on fistula related efficacy of UST in patients with active pCD treated between January 2015 and January 2020 in a real-world Danish setting. The outcomes included fistula response defined as a combination of physician's objective assessment and patient's subjective response and fistula remission defined as healing with no secretion or symptomatic activity and were assessed at week 8, week 24 and week 52. Data from the follow-ups were normally distributed according to Shapiro Wilk tests and consequently compared to baseline data through paired T-tests.

Additionally, we conducted a systematic review and meta-analysis of the current literature including our own data until April 2020 in Pubmed and EMBASE according to the Cochrane guidelines and PRISMA method. The results were analyzed using the DerSimonian and Laird random-effect models.

Results: A total of 18 patients had active pCD at initiation of UST therapy at our two large IBD centers and all were included in this study. The patients were refractory to a median of 3 (IQR 2-4) prior biologic therapies. A total of nine patients received UST as monotherapy, while the others received concomitant azathioprine (3), systemic steroids (2), antibiotics (1) methotrexate (1) and 6-mercaptopurine (1). Prior to UST initiation, 8/18 patients had received fistula related surgery, of which five patients still had a seton placement at initiation of UST therapy. The fistula systems were classified as complex in 10 patients by either MR or transrectal ultrasound assessment.

At week 8, 3/18 patients had fistula response while this proportion increased to 6/12 at week 24. However, none of our patients experienced complete fistula remission during these follow-ups. At week 52, only one patient terminated UST therapy due to non-response, while 7/11 had a response. At this time point remission could not be assessed with accuracy. During the follow-ups, only one patient required fistula excision while none of the patients required CD related hospitalization or experienced adverse events to UST.

From the systematic review of the existing literature, a total of 1,807 studies were assessed of which seven studies with 127 patients in total describing the efficacy of UST in pCD were eligible for inclusion. According to the meta-analysis, fistula response occurred in 36.5% (95%CI 20.2%-56.7%, $I^2=74\%$) of the patients at week 8 while 17.1% (95%CI 8.1%-32.7%, $I^2=45\%$) achieved fistula remission. At week 24, fistula response occurred in 39.2% (95%CI 23.1%-58.1%, $I^2=66\%$) while fistula remission occurred in 27.6% (95%CI 15.5%-44.2%, $I^2=40\%$). Due to the small sample sizes, data from week 44 in Sands' post hoc study were included in the meta-analysis of response at week 52. At this time-point, fistula response occurred in 68.0% (95%CI 53.3%-79.8%, $I^2=0\%$) but no study reported remission rates.

Conclusion: This double center cohort study combined with a meta-analysis of the current evidence shows promising short- and long-term efficacy and safety of UST in patients with pCD. However, given the small number of studies and heterogeneity in study designs, a larger and randomized trial must confirm these results.

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Disclosure: Nothing to disclose

P0607

CLINICAL AND PHARMACOKINETIC IMPACT OF METHYLPREDNISOLONE PREMEDICATION WITHDRAWAL IN INFLAMMATORY BOWEL DISEASE PATIENTS ON MAINTENANCE THERAPY WITH INFLIXIMAB

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Introduction: There are some data suggesting that premedication with intravenous methylprednisolone (mPDLN) might prevent antibodies to infliximab (ATI) formation in patients with inflammatory bowel disease (IBD) starting infliximab (IFX) therapy. On the other side, ATI seem to develop mainly within the first year of IFX therapy.

Aims & Methods: We sought to assess the impact of mPDLN premedication withdrawal on IFX trough levels (ITL), ATI formation and clinical outcomes. All IBD patients on maintenance IFX therapy with concomitant use of immunosuppressants for at least 1-year, with mPDLN premedication from the first IFX infusion and without any IFX-related acute infusion reaction (AIR) were included and prospectively followed for at least 1 year after mPDLN premedication withdrawal (Time 0). Clinical disease activity, changes in IBD therapy and AIR were recorded during follow-up. Biological parameters (C-reactive protein [CRP] and faecal calprotectin [FC]), and pharmacokinetic data (ITL and ATI) were measured and registered prior to mPDLN withdrawal (Time -1; 16 weeks before withdrawal) and at weeks 16 and 32 of follow-up (Time 1 and 2) in alternate IFX infusions.

Results: Among 100 IBD patients on active IFX therapy, 32 met the inclusion criteria. All patients but two had concomitant therapy with thiopurines. Mean duration of IFX therapy at the time of mPDLN withdrawal was 56.5 ± 41.9 months. No ITL variation was observed before and after mPDLN withdrawal (2.2±1.8 ug/mL at Time -1 vs 2.2±2.2 ug/mL at Time 2). Before mPDLN withdrawal, 11 patients had low-titer ATI (< 10ng/mL)

and 2 patients had high titer ATI (>20ng/mL). After mPDLN withdrawal, 8 of these 13 patients exhibited persistent ATI at similar titers. Additionally, 2 patients developed transient ATI, and 2 developed low-titer ATI at Time 2. No changes in biological activity was evidenced after mPDLN withdrawal (mean CRP levels: 4.4±6.8 mg/L at Time -1 vs 4.9±6.8 mg/L at Time 2; FC levels: 167.1±181.8 mg/kg at Time -1 vs 158.2±227.7 mg/kg at Time 2). Two patients required IFX dose escalation (both ATI positive at Time 0, with further disappearance of ATI). Only 1 patient developed perianal disease requiring surgery. No AIR was observed during follow-up.

Conclusion: IBD patients on maintenance treatment with infliximab and premedication with mPDLN for more than 1 year, mPDLN withdrawal was not associated with ATI formation or infusion reactions, and had no impact on ITL or IFX loss of response.

Disclosure: Nothing to disclose

P0608

PERIANAL CROHN'S DISEASE IN CHILDREN IS ASSOCIATED WITH MORE HOSPITALIZATIONS AND SURGERIES DESPITE HIGHER UTILIZATION OF IMMUNOMODULATORS AND BIOLOGICS: A REPORT FROM THE EPIIIRN COHORT

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Introduction: Perianal disease is recognized as a predictor of poor outcomes in pediatric Crohn's disease (CD), possibly indicating early biologics use. However, limited data exist to support this notion in children. We thus aimed to explore the incidence of simple and complicated perianal CD (PCD) and its association with disease outcomes, within the validated epiIIRN cohort which includes clinical and accurate drug prescription data on all IBD patients in Israel (n=45,074).

Aims & Methods: The current analysis was performed on IBD patients from the two largest Health Maintenance Organizations (HMOs), covering 78% of the Israeli population. First, we developed and validated specific algorithms to identify patients with PCD and to differentiate simple from complex disease, after establishing by chart reviews two reference cohorts of true positive (TP, patients with perianal abscess/fistula classified as simple or complicated), and true negatives (TN) of CD patients without perianal disease. We then applied the algorithms on the epiIIRN cohort for retrieving CD patients who developed PCD. Random charts were reviewed to re-validate the PCD diagnosis. The two cohorts (i.e. those with and without PCD) were linked to the National Israeli Registries from the Minister of Health that record real-life reports of all hospitalizations and surgeries in Israel.

Results: The chosen algorithm included patients with at least one perianal-related ICD code, procedure or surgery (sensitivity/specificity 75%/96% for identifying PCD, and 72%/74% for differentiating complicated vs simple PCD). A total of 2,120 children with CD were included (42% females, age at diagnosis 14.6±6.0 years), with a median follow-up of 6.4 (IQR 3.0-10.3) years. PCD was diagnosed in 164 (7.7%) by 18 years of age and in 297 (14%) in total, of whom 139 (7%) with complicated PCD. The risk for PCD was similar in children (297/2120 (14%)) and adults (2,318/17,444

(13%); OR 1.06 (95%CI 0.8-1.2)), and higher in males (201/1224 (20%)) vs. females (96/898 (11%); OR=1.7 (95%CI 1.5-2.0)). PCD patients were treated more often with biologics and thiopurines, especially those with complicated perianal disease (Figure). Despite higher utilization of drugs, PCD patients had more hospitalizations by the last follow-up (median 1 (IQR 0-5), 4 (0-10) and 12 (4-23) in non PCD, simple PCD and complicated PCD, respectively, $P < 0.001$) and more IBD-related bowel surgery (8%, 18% and 31%, respectively, $P < 0.001$).

Conclusion: Despite higher utilization of immunomodulators and biologics, children with PCD are at increased risk for hospitalizations and surgeries. PCD is a strong predictor of disease course, especially complicated PCD, and thus should prompt early intensified treatment and close monitoring.

Disclosure: DT received last 3 years consultation fee, research grant, royalties, or honorarium from Janssen, Pfizer, Hospital for Sick Children, Ferring, Abbvie, Takeda, Biogen, Neopharm, Uniliver, Atlantic Health, Shire, Celgene, Lilly, Roche

P0609

EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB IN BIOLOGIC-NAÏVE PATIENTS: REAL-WORLD DATA FROM THE SICILIAN NETWORK FOR INFLAMMATORY BOWEL DISEASES (SN-IBD)

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Introduction: Biologic-naïve patients treated with Vedolizumab (VDZ) are largely underrepresented in real-world cohorts.

Aims & Methods: We performed a multicentre, observational, cohort study on the effectiveness and safety of VDZ as treatment for Crohn's disease (CD) and ulcerative colitis (UC) among biologic-naïve subjects. Data of consecutive biologic-naïve patients with CD and UC treated with VDZ from July 2016 to December 2019 were extracted from the cohort of the Sicilian Network for Inflammatory Bowel Disease (SN-IBD). The primary outcome was the clinical response at 14 and 52 weeks.

Results: 172 consecutive patients (CD: n=88; UC: n=84; median age 66.0 years) were included, with a median follow-up of 58.8 weeks. After 14 weeks, a clinical response was reported in 68.2% of patients with CD and 67.9% of patients with UC treated with VDZ, including 45.5% patients in the CD group and 46.4% patients in the UC group who achieved steroid-free remission. After 52 weeks, a clinical response was reported in 77.4% of CD and in 73.8% of UC patients treated with VDZ, including 59.7% patients in the CD group and 60.7% patients in the UC group who achieved steroid-free remission. All differences between CD and UC were not statistically significant. Cox survival analysis showed no significant difference in the probability of treatment discontinuation between CD and UC patients (log-rank $p=0.73$).

Conclusion: This large, real-world, multicenter study demonstrated the effectiveness and safety of VDZ as a first-line biologic, showing high rates of clinical response and steroid-free remission at both induction and maintenance.

Disclosure: Fabio Salvatore Macaluso served as an advisory board member and/or received lecture grants from AbbVie, Biogen, MSD, Pfizer, and Takeda Pharmaceuticals. Walter Fries served as an advisory board member and/or received lecture grants from AbbVie, Biogen, MSD, Pfizer, Mundipharma, Zambon, Janssen, Sandoz, and Takeda Pharmaceuticals. Sara Renna served as an advisory board member for AbbVie and MSD Pharmaceuticals, and received lecture grants from AbbVie, MSD and Takeda Pharmaceuticals. Maria Cappello served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Chiesi, and Takeda Pharmaceuticals. Ambrogio Orlando served as an advisory board member for AbbVie, MSD, Janssen, Pfizer, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Sofar, Chiesi, Janssen, Pfizer, and Takeda Pharmaceuticals.

P0610

SYSTEMIC AND ORALLY ADMINISTRATION OF AC2-26 LOADED NANOPARTICLES INDUCES ANASTOMOTIC HEALING IN A MODEL OF LOCALLY INDUCED TNBS COLITIS

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Introduction: Inflammatory bowel diseases (IBD) are characterized by recurrent episodes of severe diarrhea and abdominal pain [1]. Up to 80% of patients with IBD have to undergo surgery at least once in their lifetime. Following bowel resection, bowel continuity is restored by a surgical suture (anastomosis). Disturbed anastomotic healing is associated with significant morbidity and still occurs in up to 20% of cases. Anti-inflammatory treatment by Annexin A1 or its functional peptide Ac2-26, respectively, has shown the potential to improve severity of intestinal colitis [2].

Aims & Methods: This project aims to analyze the effect of systemic and oral administration of Ac2-26 loaded nanoparticles (Ac2-26-NP) on anastomotic healing during locally induced trinitrobenzene sulfonic acid (TNBS) colitis. All animal experiments were approved by the local animal welfare committee. After cutaneous presensitization with TNBS for 6 days, colitis was induced by intrarectal administration of TNBS. Using microsurgical technique, an end-to-end anastomosis with 12 single stitches was performed at the day after induction. Collagen IV targeted nanoparticles loaded with Ac2-26 were synthesized as described before [1] for systemic administration and additionally coated with pectin for oral administration, to allow gastric passage and release in the colon by microbial pectinase activity. Treatment groups received perioperative intraperitoneal or oral administration of Ac2-26-NP every 3.5 days throughout the whole procedure. Severity of colitis was examined by the disease activity index, comprising weight loss, blood in stool and stool consistency. Anastomotic healing was evaluated at postoperative day 3 and 7 using anastomotic bursting location.

Results: Treatment with TNBS induced marked manifestations of colitis in the distal colon and at the anastomotic site and impaired postoperative weight recovery. Perioperative systemic administration of Ac2-26-NP resulted in significantly reduced postoperative weight loss compared to control ($p=0.047$). Perioperative oral administration of Ac2-26-NP showed

a significant improvement of the disease activity index at the day of operation ($p=0.001$). The DAI at postoperative day 3 and 7 in oral and systemic treatment groups and the bursting location at postoperative day 7 did not differ between the groups, respectively.

Conclusion: Systemic administration of Ac2-26-NP improved perioperative recovery while oral administration was acting locally by improving colitis activity. Anastomotic stability was not affected by the treatment approaches. Thus, a combined oral and systemic treatment approach could be a promising perioperative treatment strategy for IBD patients, due to its ability to improve colitis activity and postoperative recovery without deterioration of anastomotic stability.

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Disclosure: Nothing to disclose

P0611

CLINICAL RESPONSE TO AZATHIOPRINE IS ASSOCIATED WITH SPECIFIC METABOLIC SHIFT TOWARDS THIOGUANINE DI- AND TRI-PHOSPHATES

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Introduction: Thiopurines represent an effective therapeutic modality for inflammatory bowel disease (IBD) available at relatively low cost but efficacy of these small molecules varies depending on patient's individual metabolic profile. Therapeutic drug monitoring (TDM) of thiopurines has been proposed as a potentially effective tool in optimizing therapy of IBD but its clinical applicability is not clear. Various analytical methods have been used for TDM of thiopurines providing thus far conflicting results. Differences in analytical procedures used in clinical studies of thiopurines TDM may account for the observed controversies.

We have previously validated protocol for sample preparation and analytical procedure assessing 12 thiopurines metabolites. In the present pilot study, we use this protocol to determine the differences in the respective metabolites between IBD patients responding and non-responding to the most commonly used thiopurine, azathioprine (AZA).

Aims & Methods: IBD patients treated with stable dose of AZA for a minimal period of 6 months were eligible for the study. Basic demographics and response to AZA were noted. The peripheral blood samples were prepared according to the previously validated protocol and analyzed by ion-exchange liquid chromatography hyphenated with tandem mass spectrometry to determine twelve AZA metabolites. Metabolic shift was determined as the ratio of thioguanine 5'-monophosphate (TGMP) and thioinosine 5'-monophosphate (TIMP) vs. respective methylated metabolites (6-methyl 5'-diphosphate - MeTGDP; 6-methyl 5'-triphosphate - MeTGTP; 6-methylthioinosine 5'-diphosphate - MeTIDP and 6-methylthioinosine 5'-triphosphate - MeTITP). The differences in respective ratios were analyzed statistically using an unpaired t-test.

Results: In total, 23 IBD patients using thiopurines were included (11 men, median age 35 years, range 23-80). Four patients were on dose of 2-2.5mg/kg a day, thirteen 1-1.9mg/kg and six had the dose of up to 0.9mg/kg; the dose was reduced due to side effects, mostly leukopenia. The majority (17

patients) were using co-medication with 5-aminosalicylates, five patients were using concomitant infliximab, three vedolizumab. Out of these 23 patients, twelve were responders to azathioprine.

Although in all samples methylated metabolites were determined, the metabolomes of respective patients varied substantially with regards to predominantly methylated metabolite. Concerning clinical response to AZA, responders had significantly higher ratio of TGMP/MeTGDP and TGMP/MeTGTP compared with non-responders ($p=0.0479$ and $p=0.0232$, respectively). There were no differences in other metabolites with regards to clinical response.

Conclusion: In IBD patients, metabolic profile of azathioprine shows great interindividual variability at the level of respective metabolites. Clinical response to azathioprine is associated with decreased methylation of two specific metabolites, thioguanine di- and tri-phosphates.

References: Pecher D, Dokupilova S, Zelinkova Z et al. Analytical and Sample Preparation Protocol for Therapeutic Drug Monitoring of 12 Thiopurine Metabolites Related to Clinical Treatment of Inflammatory Bowel Disease. *Molecules*. 2018;17;23(7).

Disclosure: Nothing to disclose

P0612

EFFECTIVENESS OF USTEKINUMAB ON CROHN'S DISEASE ASSOCIATED SPONDYLOARTROPATHY

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Introduction: The efficacy of Ustekinumab (UST) on Crohn's disease (CD) associated spondyloarthropathy (SpA) was evaluated neither in randomized controlled trials nor in real-world studies.

Aims & Methods: Web-based data from the cohort of the Sicilian Network for Inflammatory Bowel Disease (SN-IBD) were extracted to perform a multicentre, real-world assessment of the effectiveness of UST on CD-associated SpA. All consecutive CD patients with active SpA at the initiation of the treatment with UST from January 2019 (the date on which the drug became available for clinical practice in Sicily) to August 2019 were extracted from the SN-IBD cohort. The study outcomes were evaluated at 8 and 24 weeks. The primary outcome was the articular response, defined as the disappearance of objective signs of arthritis (swelling and/or articular stiffness) and resolution of pain. As ancillary end-points, the clinical response (reduction of Harvey-Bradshaw Index ≥ 3 compared with baseline with a concomitant reduction of at least $\geq 50\%$ of steroid dosage compared with baseline) and the steroid-free remission (Harvey-Bradshaw Index < 5 without steroids use) were assessed.

Results: Out of 131 total patients treated with UST, 30 consecutive patients (22.9%) had active SpA at baseline (axial SpA: 3/30; peripheral SpA: 18/30; axial plus peripheral SpA: 9/30). After 8 weeks, 10 patients (33.3%) report-

ed an articular response [0/3 patients with axial SpA, 7/18 patients (38.9%) with peripheral SpA, and 3/9 patients (33.3%) with axial and peripheral SpA]. After 24 weeks, 13 patients (43.3%) had an articular response [0/3 patients with axial SpA, 10/18 patients (55.5%) with peripheral SpA, and 3/9 patients (33.3%) with axial and peripheral SpA]. None of these 13 responders was taking systemic steroids at 24 weeks. The concomitant presence of a clinical response on intestinal symptoms was associated with the articular response at 24 weeks at univariable analysis (OR 5.14, CI 1.09–32.70, $p=0.038$).

Conclusion: UST obtained a response on articular symptoms in nearly half of the patients with CD and active SpA at baseline after 24 weeks. The rate of response was higher in case of peripheral arthropathy. The articular response was associated with the clinical response on intestinal symptoms.

Disclosure: Fabio Salvatore Macaluso served as an advisory board member and/or received lecture grants from AbbVie, Biogen, MSD, Pfizer, and Takeda Pharmaceuticals. Walter Fries served as an advisory board member and/or received lecture grants from AbbVie, Biogen, MSD, Pfizer, Mundipharma, Zambon, Janssen, Sandoz, and Takeda Pharmaceuticals. Maria Cappello served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Chiesi, and Takeda Pharmaceuticals. Sara Renna served as an advisory board member for AbbVie and MSD Pharmaceuticals, and received lecture grants from AbbVie, MSD and Takeda Pharmaceuticals. Ambrogio Orlando served as an advisory board member for AbbVie, MSD, Janssen, Pfizer, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Sofar, Chiesi, Janssen, Pfizer, and Takeda Pharmaceuticals.

P0613

ITALIAN REAL-LIFE STUDY EVALUATING THE LONG-TERM EFFECTIVENESS OF VEDOLIZUMAB FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab (VDZ) is approved for the treatment of Ulcerative Colitis (UC) and Crohn's disease (CD). Real-world data showed effectiveness and safety confirming those reported in clinical trials. The aim of our study is to evaluate the effectiveness and safety of VDZ in a large real-life cohort, with a follow-up on therapy up to 2 years.

Aims & Methods: The Long-term Italian Vedolizumab Effectiveness (LIVE) study included CD and UC patients started on VDZ from April 2016 to June 2017 at 47 centers of the Italian Group for the study of Inflammatory Bowel Disease (IG-IBD). Patients were prospectively followed-up to June 2019. Co-primary endpoints were to evaluate cumulative VDZ treatment persistence and safety.

Results: This preliminary analysis involves 1111 adult patients (564 CD and 547 UC). Mean age was 47.6 years-old $\pm$ SD 16 (46.5 $\pm$ 16 for CD and 48.8 $\pm$ 16 for UC) and mean disease duration at baseline was 11.8 years $\pm$ SD 8.8 (13.2 $\pm$ 9.5 for CD, 10.4 $\pm$ 7.8 for UC). One-hundred and ninety-eight patients (17.8%) were $\geq$ 65 years-old at enrollment and 90 patients (8.1%) had a history of a previous cancer. VDZ was used as first biologic therapy in 256 patients (23%, 101 CD and 155 UC). The majority of CD patients had an ileo-colonic location (317, 56.2%) and a stricturing behavior (273, 48.4%). Three-hundred and ten UC patients (56.7%) had extensive colitis. Extra-intestinal manifestations were reported in 265 patients (23.9%). Moderate-to-severe endoscopic activity was present in 82.6% of CD and in

93.4% of UC, according to Simple Endoscopic Score for CD (SES-CD) and endoscopic Mayo score, respectively. Cumulative VDZ treatment persistence at 12 and 24 months was 74.5% (74.6% for CD and 74.3% for UC) and 57.3% (54.5% for CD and 60% for UC), respectively; mean therapy duration before withdrawal was 49.4 $\pm$ 31.4 weeks. A significant longer persistence was observed among biologic naïve patients ($p=0.009$, mean duration 82.4 $\pm$ 34.7 weeks in naïve patients vs 77.4 $\pm$ 25.4 weeks in experienced patients). 45.4% (229 CD and 273 UC), 8.2%, 8.7% and 8.4% of patients were on concomitant steroids at baseline, at 6, 12, and 24 months, respectively. Clinical remission at 12 and 24 months was achieved in 39% (206 CD and 227 UC) and in 37.4% (184 CD and 231 UC) of patients. Mean C-reactive protein was 14.2 mg/l $\pm$ SD 20.1 (15.5 $\pm$ 19.8 in CD and 13 $\pm$ 20.4 in UC) at baseline and dropped to 8 mg/l $\pm$ SD 14 (10.2 $\pm$ 18 in CD and 5.9 $\pm$ 8.1 in UC) at 12 months and to 5.5 mg/l $\pm$ SD 8.8 (6.4 $\pm$ 9.8 in CD and 4.6 $\pm$ 7.7 in UC) at 24 months. Eighty-five CD patients (15.1%) and 166 UC patients (30.3%) achieved endoscopic remission (SES-CD $<$ 3 or endoscopic Mayo score = 0, respectively) within the study period. Two-hundred and sixty-four adverse events were reported, but only 90 (28 infections, 22 new cancer/dysplasia, 19 arthritis) of them (8.1% of patients) led to VDZ withdrawal.

Conclusion: In this preliminary analysis of the largest reported real-world cohort of Inflammatory Bowel Disease patients treated with VDZ, up to 60% of patients persisted on therapy with a favorable safety profile after 2 years of follow-up.

Disclosure: Nothing to disclose

P0614

SPOSAB ABP 501 - A SICILIAN PROSPECTIVE OBSERVATIONAL STUDY OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH ADALIMUMAB BIOSIMILAR ABP 501

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Introduction: Clinical data on the use of Adalimumab (ADA) biosimilar ABP 501 in inflammatory bowel disease (IBD) are lacking.

Aims & Methods: SPOSAB ABP 501 is a multicenter, observational, prospective study performed among the cohort of the Sicilian Network for Inflammatory Bowel Disease (SN-IBD). All consecutive patients with Crohn's Disease (CD) or Ulcerative Colitis (UC) treated with ABP 501 from the introduction of the drug in Sicily (February 2019) to February 2020 (12 months) were enrolled. Patients were divided into 3 groups (group A: naïve to ADA and naïve to anti-TNFs; group B: naïve to ADA and previously exposed to anti-TNFs; group C: switch from ADA originator to ABP 501). The primary end-point was the assessment of safety, in terms of rate of serious adverse

events (SAEs). Secondary end-point was the evaluation of effectiveness, in terms of clinical response and steroid-free clinical remission at 12 weeks for group A and B, and as treatment persistency for all 3 groups.

Results: 559 patients (median age 39 years; CD 88.0%, UC 12.0%) were included [group A: 189 (33.8%); group B: 30 (5.4%); group C: 340 (60.8)]. Overall, the mean follow-up was 8.7 months (median 10.0 months, interquartile range: 6.0-12.0 months), and the total follow-up time was 403.4 patient-years. 36 SAEs occurred in 36 patients (6.4%), with an incidence rate of 8.9 per 100 person-years (PY), and 22 of them caused the withdrawal of the drug (incidence rate: 5.5 per 100 PY). The incidence rate of SAEs was higher among patients in group A compared with group C (17.4 vs. 4.8 per 100 PY; incidence rate ratio=3.61; $p < 0.001$) and among patients in group B compared with group C (16.4 vs. 4.8 per 100 PY; incidence rate ratio=3.42; $p = 0.041$). The effectiveness of ABP 501 after 12 weeks of treatment was assessed in patients naïve to ADA (group A + B; $n = 219$): 188 patients (85.8%) had a clinical response, including 165 (75.3%) who achieved a steroid-free remission. Among the patients who responded at 12 weeks, a subsequent loss of response was reported in 17 subjects (9.0%). At the end of follow-up, 56 patients (10.0%) interrupted the treatment, with higher treatment persistency estimations for patients in group C compared with group A and B (log-rank $p < 0.001$).

Conclusion: This is the first prospective study on the use of ADA biosimilar ABP 501 in IBD. Safety and effectiveness of ABP 501 seem to be overall similar to those reported for ADA originator. Switching from originator to ABP 501 was safe and effective.

Disclosure: Fabio Salvatore Macaluso served as an advisory board member and/or received lecture grants from AbbVie, Biogen, MSD, Pfizer, and Takeda Pharmaceuticals. Walter Fries served as an advisory board member and/or received lecture grants from AbbVie, Biogen, MSD, Pfizer, Mundipharma, Zambon, Janssen, Sandoz, and Takeda Pharmaceuticals. Sara Renna served as an advisory board member for AbbVie and MSD Pharmaceuticals, and received lecture grants from AbbVie, MSD and Takeda Pharmaceuticals. Maria Cappello served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Chiesi, and Takeda Pharmaceuticals. Ambrogio Orlando served as an advisory board member for AbbVie, MSD, Janssen, Pfizer, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Sofar, Chiesi, Janssen, Pfizer, and Takeda Pharmaceuticals.

P0615

WHICH SECOND-LINE BIOLOGIC AFTER ANTI-TNF FAILURE DURING CROHN'S DISEASE: USTEKINUMAB OR VEDOLIZUMAB, A MULTICENTRE RETROSPECTIVE STUDY

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Introduction: Anti-TNF antibodies treatments are the only first-line reimbursed biologics for Crohn's disease (CD) in several countries. Recently, Vedolizumab (VDZ) and Ustekinumab (UST) were added to the therapeutic armamentarium for CD refractory to a first anti-TNF antibody. However, studies comparing these two compounds remain unavailable. Our aim was to compare their efficacy in second-line treatment in CD after failure of one TNF antagonist.

Aims & Methods: All patients with CD refractory (primary or secondary non-responders) to a first anti-TNF treatment and receiving UST or VDZ as a second biologic were included retrospectively in 10 French tertiary centres. The remission and clinical response were assessed at week 14. Population characteristics were compared by univariate analysis using the Student test or Chi 2 in an appropriate way. A multivariate logistic regression analysis was performed to assess factors associated with remission. On the long-term, the cumulative probabilities of being in remission were estimated using the Kaplan-Meier method and the associated factors using a Cox proportional risk model. The drug survival to assess efficacy as well as side effects was assessed by actuarial analysis.

Results: Among the 205 screened patients, 5 patients had no follow-up. Among the 200 Patients included (89 (45%) males, mean age of 39 years), 136 (68%) were treated with UST and 64 (32%) with VDZ. The first anti-TNF was discontinued for primary or secondary non-response in 143 (71%) patients and for side effects in 57 (29%) patients, without any difference between the anti-TNF antibody previously used. Among the 200 patients, 132 (66%) had active disease at baseline defined by a Harvey Bradshaw index above 4 associated with an increase of an objective marker (CRP, fecal calprotectin, endoscopy or imaging).

Among these 132 patients, no difference was observed on the short term at week 14, for clinical response and clinical remission according to the type of treatment: the rate of steroid free remission without positive objective marker of inflammation on the short term were 29% (UST)/38% (VDZ) ($p = 0.29$). After a mean treatment time of 73 weeks, the cumulative probabilities of being in remission at 12 months were 32% and 47% for VDZ and UST, respectively, without difference between the two group (log rang=0.95). No predictive factor of treatments efficacy was difference for both short and long term.

Overall for the 200 included patients, the drug survival was similar between the UST group and the VDZ group (log rang = 0.09). Prior optimization of the anti-TNF optimisation before the swap was associated with lower drug survival (HR=0.52 95CI(0.27-0.99), $p = 0.04$). Prior treatment with infliximab was associated with a lower vedolizumab drug survival.

Conclusion: Our results suggest that VDZ and UST have similar efficacy in the short- and long-term response when used as a second-line biologic therapy in CD refractory to a first anti-TNF antibody. These results will be complemented for the congress by the inclusion of third group treated with anti-TNF.

References: Our results suggest that VDZ and UST have similar efficacy in the short- and long-term response when used as a second-line biologic therapy in CD refractory to a first anti-TNF antibody. These results will be complemented for the congress by the inclusion of third group treated with anti-TNF.

Disclosure: Nothing to disclose

P0616

EFFICACY, SAFETY AND DRUG SURVIVAL OF THIOGUANINE AS MAINTENANCE TREATMENT FOR INFLAMMATORY BOWEL DISEASE: A MULTI-CENTRE UK STUDY

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Introduction: Thioguanine (TG) is a thiopurine which has been used for patients with inflammatory bowel disease (IBD) who have failed azathioprine (AZA) or mercaptopurine (MP) due to adverse events or suboptimal response. Its widespread use has been hampered due to concerns about nodular regenerative hyperplasia (NRH) of the liver. The aim of this study was to investigate the long-term efficacy and safety of low-dose TG therapy in IBD patients failing AZA and MP.

Aims & Methods: A retrospective multicentre study was performed in IBD patients who failed prior treatment with conventional thiopurines with or without following immunomodulation (thiopurine-allopurinol, biologicals, methotrexate, tacrolimus) and were subsequently treated with TG as rescue monotherapy between 2003 and 2019 at three hospitals in the United Kingdom. Clinical response, adverse events, laboratory results, imaging and liver biopsies were retrospectively collected.

Results: A total of 193 patients (57% female and 64% Crohn's disease) were included, with a median daily TG dose of 20 mg (range: 20-40 mg), a median treatment duration of 23 months (IQR 10 - 47) and a median follow-up of 36 months (IQR 22 - 53). The clinical response rate at 12 months was 65%, and 54% remained on TG until the end of followup. Adverse events consisted primarily of elevated liver tests (6%), myelotoxicity (7%) and rash (5%). NRH was histologically diagnosed in two patients and two other patients (1%) developed non-cirrhotic portal hypertension. The median 6-TGN and TPMT levels were 953 pmol/8x10⁵ RBC (IQR 145 - 1761) and 47 mu/L (IQR 34.5-96).

Conclusion: Long-term follow-up suggests that TG can be an effective and well-tolerated therapy in more than half of difficult-to-treat and multi-therapy failing IBD patients. Findings of this study indicate that TG can be

used safely and the occurrence of hepatotoxicity was low. The incidence rate of NRH was within the background incidence.

Disclosure: AB Bayoumy and ELSA van Liere received travel grants from TEVA. A Ansari has nothing to declare. M Simsek has received an unrestricted research grant from TEVA Pharma. CJJ Mulder has served as consultant and principal investigator for TEVA Pharma B.V. He has served as consultant and principal investigator for Takeda and TEVA Pharma B.V. He has received a (unrestricted) research grant from Dr. Falk and Takeda. NKH de Boer has served as a speaker for AbbVie and MSD and as a consultant and principal investigator for TEVA Pharma BV and Takeda. He has received unrestricted research grants from Dr. Falk, TEVA Pharma BV and Takeda.

P0617

COMBINED MEDICAL AND SURGICAL THERAPY IN COMPLEX PERIANAL CROHN'S DISEASE - EFFICACY AND PREDICTIVE FACTORS FOR THERAPEUTIC FAILURE

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Introduction: Complex perianal Crohn's disease (CD) is associated with high morbidity. Despite combined medical and surgical therapy, its approach remains challenging.

Aims & Methods: Our aim was to retrospectively evaluate its response to combined therapy and identify predictive factors for therapeutic failure. Patients with complex perianal CD treated in our hospital between 2000 and 2019 were included. Complete response was defined as complete absence of perianal drainage despite gentle finger compression and partial response as drainage reduction > 50%. Predictive factors such as gender, smoking, disease localization and rectal involvement were evaluated.

Results: 65 patients were included, being 52.3% women with a median age of 31.8 years-old. The majority (58.2%) had ileocolonic CD, 44.4% had rectal involvement and 27.3% were smokers. 6 women had rectovaginal fistulae. Initially 33.8% were treated with azathioprine in monotherapy and 67.2% with anti-TNF (61.5% infliximab; 4.7% adalimumab) with or without azathioprine. The surgical procedures performed were noncutting setons placement (66.1%), abscess drainage (56.9%), fistulotomy (14.3%), fistulectomy (7.9%) and one advancement flap (1.5%).

During follow-up (median of 11 years), the majority of patients presented a favorable response (complete in 73.8% and partial in 9%). Infliximab lead to a partial or complete response in 75% of patients and adalimumab in 57.1%, although this difference was not statistically relevant (p-value 0.211). It was necessary to switch anti-TNF therapy in 16.7% of patients due to lack of response. Although patients with rectovaginal fistulae had worse outcomes, with complete response in 50% (versus 76.2% in patients without rectovaginal fistulae), this difference was not statistically significant (p-value 0.1678).

One patient with lack of response to infliximab and adalimumab presented partial response to ustekinumab. Regarding the 11 patients with therapeutic failure, 3 underwent protective colostomy, 1 developed adenocarcinoma in a fistula tract and 1 developed anal squamous cell carcinoma. One patient developed fecal incontinence after fistulotomy.

No association was found between smoking, gender, CD localization or rectal involvement and therapeutic failure.

Conclusion: Although perianal CD treatment remains challenging, combined medical and surgical therapy proof to be successful in the majority of our patients, with few adverse events.

Disclosure: Nothing to disclose

P0618 WITHDRAWN

P0619

FIRST-LINE AZATHIOPRINE WITH ALLOPURINOL CO-THERAPY IS A PROMISING LONG-TERM TREATMENT STRATEGY FOR INFLAMMATORY BOWEL DISEASES

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Introduction: Beneficial response from first-line immunosuppressive azathioprine (AZA) in inflammatory bowel disease (IBD) patients is low due to high rates of adverse events. Co-administrating allopurinol has been reported to improve tolerability.

Aims & Methods: The aim of this study was to compare the long-term efficacy and safety of first-line low-dose azathioprine and allopurinol (LDAA) with first-line AZA monotherapy (AZAm) in IBD patients unguided by metabolites.

Medical records from a single centre were reviewed retrospectively. Clinical benefit was defined as: ongoing use of therapy without initiation of steroids, biologics or IBD-surgery. Secondary outcomes included disease activity indices, endoscopic findings, steroid-withdrawal, CRP and adverse events.

Results: 166 LDAA and 118 AZAm patients (≥90% having active disease, median follow-up 25 and 27 months respectively) were included. Clinical benefit was higher in the LDAA cohort at both 6 months (74% versus 53%, $p=0.0004$) and 12 months (54% versus 37%, $p=0.01$). Sustained clinical benefit during a median of 36 months was observed in 37% of LDAA patients (compared to 24% of AZAm, $p=0.04$). In the AZAm cohort the median dose tolerated was 1.83 mg/kg (73% of most effective dose) and 45% discontinued due to intolerance. Occurrence of myelotoxicity was similar in LDAA versus AZAm patients ($p=0.17$). Myelotoxicity and elevated liver function tests led to LDAA withdrawal in only 2% for both. Increasing allopurinol from 100 to 200-300 mg/day significantly lowered liver enzymes in 83% of LDAA patients with hepatotoxicity.

Conclusion: Optimisation of AZA therapy for IBD is needed as poor outcomes were observed in our AZAm cohort. LDAA without metabolite monitoring may be considered standard first-line immunosuppressive therapy, as we demonstrated a long-term safe and effective profile.

Disclosure: ELSA van Liere and AB Bayoumy received travel grants from TEVA Pharma BV. C.J.J. Mulder has served as consultant and principal investigator for TEVA Pharma B.V. N.K.H. de Boer has served as consultant and principal investigator for TEVA Pharma BV and Takeda. He has served as a speaker for AbbVie, Takeda and MSD and has received unrestricted research grants from Dr. Falk and Takeda. A. Ansari has served as consultant and speaker for Dr. Falk. He has received unrestricted research grants from Janssen Cilag and MSD.

P0620

PECTIN-COATED AC2-26-LOADED NANOPARTICLES FACILITATE ANASTOMOTIC HEALING IN A MURINE MODEL OF COLONIC SURGERY DURING EXPERIMENTAL COLITIS

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Introduction: Inflammatory bowel diseases, as ulcerative colitis, are frequent. They occur with prevalence rates up to 300 / 100,000 people in the western world [1]. They are marked by severe symptoms, such as recurrent diarrhea, weight loss and pain. Up to 80% of patients suffering from inflammatory bowel disease undergo surgery once in their lifetime. Following resection of the affected intestinal segment, anastomotic leakage still occurs in up to 20% of cases and is further promoted by mucosal inflammation in those patients. Anastomotic leakage is a life-threatening complication, leading to intraabdominal sepsis and death in 20% of cases. Anti-inflammatory treatment by Annexin A1 promoting the resolution of inflammation has shown the potential to improve intestinal colitis [2, 3].

Aims & Methods: The aim of this project is to evaluate the therapeutic potential of perioperative oral administration of a novel formulation of pectin-coated nanoparticles containing Ac2-26, the functional peptide of Annexin A1, to promote intestinal wound healing during colitis conditions. Experimental colitis was induced by dextran sodium sulfate in drinking water prior to intestinal surgery in a murine model. After 7 days conventional drinking water was offered followed by surgical transection of the descending colon and restoration of bowel continuity by 12 single stiches in a microsurgical technique. Collagen IV targeted nanoparticles loaded with Ac2-26 were synthesized as described before [4] and additionally coated with pectin to allow gastric passage and release in the colon by microbial pectinase activity. Nanoparticles were administered by oral gavage every 3.5 days throughout the whole procedure (initiation of colitis to evaluation). The mice were sacrificed at postoperative day (POD) three or seven, respectively. Severity of colitis and anastomotic healing were evaluated by disease activity index, consisting of weight loss, blood in stool and stool consistency. Anastomotic healing was scored by colonoscopy, scoring of abdominal adhesions and bursting pressure of the anastomosis.

Results: Oral Ac2-26-nanoparticle treatment resulted in a significant improvement of disease activity at POD 3 (0.56 vs. 0.94, $p=0.02$) and POD 7 (0.50 vs. 1.00, $p=0.02$), while the preoperative disease activity index did not differ (0.59 vs. 0.68, $p=0.52$) between the groups. Wound closure score was significantly improved in endoscopic examination by nanoparticle treatment at POD 3 (0.89 vs. 2.33, $p=0.02$) and POD 7 (0.90 vs. 2.46, $p=0.0002$). Less adhesions occurred in the treatment group at POD 3 (2.33 vs. 3.58, $p=0.0037$) and POD 7 (3.60 vs. 5.09, $p=0.02$), which is also a marker for improved intestinal wound closure. Bursting pressures and body weight curves showed no significant differences between the groups.

Conclusion: Oral treatment with Ac2-26 encapsulated in pectin-coated Col-IV targeted nanoparticles has a positive impact on intestinal anastomotic wound healing. The effect is predominantly local as postoperative weight recovery does not differ between the groups. Thus, oral nanomedicine-based treatment with Annexin A1 might be a promising approach for perioperative treatment during colitis conditions. Pharmacokinetics and molecular mechanisms need to be further examined and require additional studies.

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Disclosure: Nothing to disclose

P0621

USTEKINUMAB IMPROVES EXTRA-INTESTINAL MANIFESTATIONS IN CROHN'S DISEASE: A POST HOC ANALYSIS OF THE UNITI STUDIES

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Introduction: UNITI-1/2 and IM-UNITI demonstrated that ustekinumab (UST) was effective in inducing and maintaining clinical remission in moderate to severe Crohn's disease (CD) patients. Although UST has proven efficacy in psoriatic arthritis treatment, no studies have assessed its effectiveness for treatment of extraintestinal manifestations (EIMs) in inflammatory bowel disease patients. This *post hoc* analysis aimed to evaluate the effect of UST on EIM resolution in moderate to severe CD patients at week 6 and 52 of therapy.

Aims & Methods: EIM data obtained from the YODA Project (Yale Open Data Access #2019-4104) pooled patients from UNITI-1/2 (ClinicalTrials.gov number: NCT01369329 and NCT01369342), and IM-UNITI (NCT01369355). The analysis included 941 eligible patients for UST induction and 260 eligible patients for maintenance. The prevalence, resolution (absence of EIM), *de novo* development for any EIM or specific EIM (anal disease, aphthous stomatitis, arthritis/arthralgia, erythema nodosum, fever >100°F, iritis/uveitis, primary sclerosing cholangitis, pyoderma gangrenosum) was evaluated at week 6 and 52 of UST therapy. EIMs were measured using the Crohn's Disease Activity Index (CDAI). McNemar's test was used to evaluate the proportion of patients who reported active EIMs at week 6 and 52 after UST treatment compared to baseline.

EIM	Baseline (%)	Prevalence at Week 6 (%)	De Novo EIM at Week 6 (%)	P-value
Anal fissure, fistula or abscess	155 (16.5)	126 (13.4)	8 (0.9)	0.001
Aphthous stomatitis	37 (3.9)	6 (0.6)	10 (1.1)	0.002
Arthritis/arthralgia	471 (50.1)	320 (34.0)	35 (3.7)	<0.0001
Erythema nodosum	28 (3.0)	9 (1.0)	1 (0.1)	0.002
Fever >100°F	94 (10.0)	6 (0.6)	22 (2.3)	<0.0001
Iritis/uveitis	23 (2.4)	8 (0.9)	4 (0.4)	0.019
Primary sclerosing cholangitis	8 (0.9)	7 (0.7)	0	1.000
Pyoderma gangrenosum	5 (0.5)	4 (0.4)	1 (0.1)	1.000
Total	821	486	81	<0.0001

[Prevalence and De Novo Development by Week 6 of UST Induction]

Results: At baseline, 66.4% (625/941) patients who received UST induction had 821 total EIMs. The prevalence of patients with EIMs was 49.7% (486/941), resolution of total EIMs was 40.8% (335/821), and *de novo* development of patients with EIMs was 8.6% (81/941) compared to baseline

($p < 0.0001$). Compared to baseline, the prevalence was 20.2% (53/263), resolution was 76.9% (176/229) ($p < 0.0001$) and *de novo* development was 6.8% (18/263) and 2.2% (5/263) at weeks 6 and 52, respectively (Table 1). UST induction and maintenance therapy demonstrated initial and sustained improvement in the prevalence and resolution of all EIMs, except for iritis/uveitis, primary sclerosing cholangitis and pyoderma gangrenosum compared to baseline.

Conclusion: This analysis of the CD patients enrolled in the UNITI trials demonstrates that UST shows improvement in most EIMs by week 6 with sustained response to 52 weeks.

Disclosure: Nothing to disclose

P0622

INCREASED RELAPSE RATE AFTER DISCONTINUATION OF IMMUNOMODULATOR MONOTHERAPY BUT NOT AFTER WITHDRAWAL FROM COMBINATION REGIMEN IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Withdrawal of treatment is a common therapeutic issue in patients with longstanding stable remission in inflammatory bowel disease (IBD).

Aims & Methods: To evaluate the relapse rate in patients with quiescent IBD after cessation of biologic or immunomodulator (IM) therapy. We searched five databases (CENTRAL, EMBASE, Scopus, Web of Science, PubMed) for randomized controlled trials (RCT) evaluating disease relapse after withdrawal of monotherapy or a drug from combination therapy in Crohn's disease (CD) or ulcerative colitis (UC). Risk ratios (RR) were calculated with 95% confidence intervals (CI) with the random effect model. Statistical heterogeneity was assessed using χ^2 and I^2 statistics.

Results: Nine RCTs (535 patients with IBD) were included in the meta-analysis. Withdrawal of IM monotherapy resulted in a significantly higher risk of relapse within 24-months of follow-up compared to ongoing therapy in CD, but not in UC patients ($RR_{CD} = 2.06$, CI: 1.53-2.77, $p < 0.001$ and $RR_{UC} = 1.39$, CI: 0.85-2.26, $p = 0.189$, respectively). Discontinuation of an IM from combination with biologics did not show a higher risk of relapse than continuation of both drugs ($RR = 1.31$, 95% CI: 0.81-2.14, $p = 0.275$). According to the trial sequential analysis, no further studies are needed to confirm significant results on relapse rates after withdrawing IM monotherapy in patients with CD.

Conclusion: High quality of evidence suggests that continuing IM monotherapy should remain the preferred approach among patients with CD, although long-term toxicity is a major concern. However, further large RCTs are warranted in UC and combination regimen with biologics.

Disclosure: Nothing to disclose

P0623

COMPARISON OF SERUM ADALIMUMAB TROUGH LEVELS IN 40MG WEEKLY VS 80MG EVERY TWO WEEKS INTENSIFICATION REGIMES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Adalimumab treatment often needs intensification, currently it can be done with two different regimes, 40 mg every week or 80 mg every other week (eow). Little is known about the pharmacodynamics of this different doses and patient preferences.

Aims & Methods: The aim of our study is to compare trough levels in the two Adalimumab intensification doses: 40 mg weekly and 80 mg every two weeks.

Methods: Patients with inflammatory bowel disease treated with original adalimumab in an intensified weekly dosage for at least 4 weeks were included. Adalimumab trough levels and antibodies were measured by ELISA assay every 2 weeks.

Patients were randomized to 40 mg every week (group A) or 80 mg eow (group B). After 6 weeks patients in the 40 mg arm were changed to 80 eow dose. Primary endpoint was variation from basal in trough levels at week 6. Secondary endpoints were antibody development, quality of life (IBDQ questionnaire), drug satisfaction (TSQM questionnaire). Harvey Bradshaw / SCCAI index and CRP, albumin, hemoglobin and calprotectin were also measured. Protocol was approved by the local ethics committee.

Results: 11 patients were enrolled, 10 of them were randomized, 5 in each arm. 1 patient was prematurely withdrawn from the study because of disease worsening and treatment change. That patient was followed for safety population.

Patients were 40% female, 60% male, mean age was 51.8 y and 30% had UC and 70% EC.

No significant differences in Basal characteristics were found, specifically adalimumab was the first antiTNF treatment in 3/5 in Group A (60%) vs 2/5 Group B (40%) $p=0.52$ and concomitant immunosuppressants were used in 3/5 group A (60%) vs 3/5 (60%) group B $p=1$. Basal trough levels showed no significant differences between groups $15.2 \pm 5.6 \mu\text{g/ml}$ vs $17.8 \pm 12.3 \mu\text{g/ml}$ $p=0.68$.

At week 6 No significant differences between groups were found in change of adalimumab levels vs baseline $0.5 \pm 3.9 \mu\text{g/ml}$ vs $-1 \pm 5.7 \mu\text{g/ml}$; $p=0.6$. Also no differences were found in CRP, hemoglobin or calprotectin or IBDQ score 182 ± 25.9 vs 178.2 ± 31.7 $p=0.86$ and TSQM 56.6 ± 17.2 vs 45.4 ± 6.6 .

No patient developed antibodies during the study.

After w6 patients receiving 40mg/w Trough levels changed to 80mg/eow and were followed until w12. Trough levels at w12 were not different from w6 $13.9 \pm 3.3 \mu\text{g/ml}$ vs $12.4 \pm 0.9 \mu\text{g/ml}$. Also no differences were found in any other variable.

Patients were asked about their personal preference and 9/10 (90%) preferred the 80 mg/eow dose.

No significant adverse events occurred during the study.

The study was early terminated because of COVID19 pandemic that prevented study procedures to be followed as planned.

Conclusion: No significant differences were found in Adalimumab trough levels between 40mg/w vs 80 mg/eow in a small randomized trial. Patients preferred 80 mg/eow.

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P0624

SWITCHING OUT OF CLASS IS THE MOST EFFECTIVE STRATEGY IN IBD PATIENTS WITH IMMUNOGENICITY AGAINST ANTI-TNF ANTIBODIES

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Introduction: Immunogenicity to anti-TNF agents is associated with loss of response in inflammatory bowel disease (IBD). However, the efficacy of different strategies to restore favourable pharmacokinetics and/or clinical response upon the detection of anti-drug antibodies (ADA) has not been widely studied.

We evaluated the success of different therapeutic pathways leading to clinical remission with antibody disappearance (in patients continuing the same drug), in patients with IBD.

Aims & Methods: IBD patients with ADA to infliximab (IFX) or adalimumab (ADL) were identified through an electronic database search at a single centre between 2004 and 2019. ADA were measured using a drug-sensitive assay from Sanquin laboratories: ADA>12 AU/ml were considered positive. Data concerning clinical, biochemical and endoscopic activity, medication and surgery were retrospectively and systematically collected by reviewing clinical records. Strategies that were studied included:

- 1) same dose anti-TNF continued,
- 2) dose increase of the same anti-TNF,
- 3) start/optimization of immunosuppression,
- 4) combination of (2) and (3),
- 5) switch to another anti-TNF,
- 6) stop biologic treatment,
- 7) switch to out of class biologic and
- 8) surgery.

Criteria for success of a strategy were remission at 1 year on the same strategy combined with disappearance of ADA in patients continuing the same agent.

Results: Two-hundred-and-ten IBD patients (172 Crohn's disease, 35 ulcerative colitis, 3 IBD-unclassified) were included, 115 patients had IFX and 95 ADL as current anti-TNF agent. At baseline, median ADA titer was 67 (IQR 20-310) AU/ml; 54% of patients were in clinical remission. Groups were as follows:

- 1) 41/210(20%) patients continued on same dose anti-TNF,
- 2) 41/210(20%) patients were dose -intensified,
- 3) 24/210(11%) started or optimised immunomodulators
- 4) 13/210(6%) were both dose intensified and optimised immunomodulators,
- 5) 42/210(20%) switched to a different anti-TNF,
- 6) 30/210(14%) stopped biologic treatment,
- 7) 11/210(5%) switched to out another class of biological therapy and
- 8) 8/210(4%) patients had surgery.

Anti-TNF dose intensification with concomitant addition/optimisation of immunomodulators was the fastest (median 3 months (IQR 2-4,5), $p=0,004$) and most effective (73%, $p=0,007$) strategy to suppress ADA to undetectable levels. Clinical remission rates are shown in table 1. Switch to an out of class biologic was the most successful strategy in terms of improvement of clinical remission at 1 year (64%, $p=0,016$). Switch to a different anti-TNF (33%, $p=0,001$) was second best and was particularly successful (91%, $p=0,02$) in patients in clinical remission at baseline with an ADA titer ≥ 67 AU/ml. Patients that continued with same dose anti-TNF or switched to non-biological therapy were often already in clinical remission at baseline, (34/41(82,9%), and 24/30(80,0%)), but deteriorated significantly in 1 year, in 29%, ($p=0,004$) and 30% ($p=0,022$) of patients, respectively.

	Same dose anti-TNF (n=41)	Intens anti-TNF (n=41)	IM opt (n=24)	Intens anti-TNF & IM opt (n=13)	Switch anti-TNF (n=42)	Stop anti-TNF (n=30)	Out of class switch (n=11)	Surgery (n=8)
Success of strategy	54%	39%	50%	62%	60%	50%	64%	50%
Δ Clinical remission at 1 year compared to baseline	-29%	-12%	-13%	+8%	+33%	-30%	+64%	+38%

[Strategies and outcome]

Conclusion: Intensification of anti-TNF dosing with concomitant optimisation of immunomodulatory therapy is the fastest strategy to suppress ADA. Out of class switch is the most successful strategy to regain and maintain clinical remission upon detection of ADA.

Disclosure: Nothing to disclose

P0625

GASTROINTESTINAL TOXICITY DUE TO IMMUNE CHECKPOINT INHIBITORS: CLINIC EXPERIENCE IN A TERTIARY REFERRAL HOSPITAL

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Introduction: Immune Checkpoint inhibitors (ICI) are a novel group of monoclonal antibodies which are increasingly used to treat several types of cancer. These drugs enhance the antitumor response by blocking the signaling via either cytotoxic T lymphocyte antigen 4 (anti-CTLA4) or programmed cell death protein 1 (anti-PD1) which are responsible for immune tolerance pathways. This antitumoral hyperactivation derives on a wide range of toxicities. Gastrointestinal immune related adverse events (GI-IrAE) are ones of the most frequent and severe. Enterocolitis, microscopic colitis and gastritis are the usual clinical presentations. We collected the real clinical experience in a tertiary center with a multidisciplinary IrAE committee. We describe our treatment experience and the complications observed within their use.

Aims & Methods: A retrospective, descriptive and observational study was conducted in adult patients under ICI treatment (anti-CTLA4, anti-PD1 or anti-PD1L). Subjects included developed severe IrAE who required referral to the gastrointestinal unit (GIU) for treatment. We included all patients between January 2017 to January 2020, collecting the clinic, epidemiologic and evolutive data.

Results: A total of 16 patients under ICI treatment were included. The medium age was 52 (30-82), 50% were women and 50% man. 62% (n=10) were under anti-PD-1/PD1L, 12% (n=2) under anti-CTLA 4 and 25% (n=4) under combine treatment (anti-PD-1 and anti-CTLA-4). On 93% onset clinic was diarrhea grade 2 and on 6% were dyspepsia. All patients had a endoscopic, radiologic and histologic study. 75% (n=12) patients had enterocolitis (18% (n=3) microscopic colitis and 6% (n=1) gastritis). Upper gastrointestinal endoscopy was performed in 7 patients, only one with upper GI symptoms. All patients were proved to have histological inflammatory changes on the duodenum biopsies, 57% (n=4) had also visible endoscopic lesions.

The median onset of GI-IrAE were 102 days, and the interquartile range were 237 days. ICI treatment were stopped in all patients with a GI-IrAE. All patients started systemic steroids treatment, except for one patient with microscopic colitis in which we used a local action steroid (budesonide). 62% (n=10) of those patients had clinical remission with steroids. 31% (n=5) were refractory and one patient had a steroid-dependent course. All 5 patients with refractory-steroid course received anti-TNF treatment with Infliximab and approach based on therapeutic drug monitoring. One patient had complete response after one infusion. There was not clinical improvement with second and a third Infliximab infusion in the others.

Two anti-TNF refractory patients received Ustekinumab with good clinical response after one infusion. One patient received plasmapheresis therapy as concomitant treatment with clinical improvement. The patient with steroid-dependent course started Vedolizumab treatment. 18% (n=3) patients had infectious complications (aspergillosis lung-disease, *Clostridioides difficile* disease and cytomegalovirus over infection), 31% (n=5) died because of different causes (tumor progression, infectious complication or colonic perforation). Three patients had other IrAE concomitantly. We included three patients with inflammatory bowel disease under ICI treatment, one of them developed enterocolitis secondary to the treatment.

Conclusion: GI-IrAE are increasingly their incidence on clinical practice. Gastroenterologist have a important role in the manage of these patients, being necessary to create multidisciplinary committees. IBD patients under ICI treatment need a closer follow-up.

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Disclosure: not having

P0626

TREATMENT OF ANASTOMOTIC LEAKAGE FOLLOWING ILEAL POUCH ANAL ANASTOMOSIS IN UC PATIENTS, RESULTS FROM A TERTIARY REFERRAL CENTRE

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Introduction: Anastomotic leakage (AL) after restorative proctocolectomy with IPAA is a major complication occurring in up to 16% of patients, and can lead to chronic pelvic sepsis with pouch dysfunction and pouch failure on the long term. Conventional management (CM) of AL consists of a protective ileostomy and repetitive drainage of the leakcavity to obtain secondary healing, and is time-consuming with only moderate results. In recent years, early surgical closure (ESC) of AL with active drainage and surgical closure of the defect is hypothesized to be beneficial in preventing long-term complications, but has not been demonstrated yet.

Aims & Methods: The aim of this study was to compare early surgical closure of AL after IPAA surgery in UC patients with conventional management. All patients with confirmed anastomotic dehiscence after IPAA surgery between 1991 and 2018 in UZ Leuven were included. Data on patient characteristics, treatment and follow-up were extracted from electronic medical charts. Main endpoints were time to stoma closure, complications and pouch failure (defined as pouchectomy with or without redo pouch).

Results: From a total of 378 IPAA procedures, anastomotic dehiscence was confirmed in 34 patients (9.0%). From these 34 patients, 29 needed drainage of the leakcavity. From these 29 patients, 8 (27.6%) underwent ESC after Endosponge (n=6) or Pezzer (n=2) drainage and 21 patients received CM. Overall follow up was median 58.5 months (19 M in ESC and 126 M in CM group). ESC was more often performed after a modified 2-stage procedure compared to the CM group (62.5% versus 4.8%, $p = 0.004$). Median duration of treatment and time to stoma closure were shorter in the ESC group compared to CM (6.00 days versus 11.00 days, $p = 0.16$, and 106.5 days versus 133 days, $p = 0.26$ resp.). There were less early (during hospitalization) and late complications in the ESC group compared to the CM group (14.3% versus 47.6%, $p = 0.19$, and 42.9% versus 61.9%, $p = 0.42$ resp.). This results in less pouch failure in the ESC group compared to the CM group, although not significant (0% versus 23.8%, $p = 0.29$).

Conclusion: Anastomotic leakage after restorative proctocolectomy with IPAA is a feared complication and is associated with impaired functional outcomes. Our data suggest that early transanal drainage followed by surgical closure after IPAA leakage may reduce complications and thereby prevent pouch failure on the long term.

Disclosure: Nothing to disclose

P0627

RISK ASSESSMENT FOR POSTOPERATIVE RECURRENCE AFTER ILEOCOLONIC RESECTION IN CROHN'S DISEASE (ON BEHALF OF THE DUTCH INITIATIVE ON CROHN AND COLITIS (ICC))

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Introduction: Prophylactic medication to prevent postoperative recurrence (POR) after ileocolonic resection is preferably only applied in patients at high risk. According to previous publications, patients with active smoking, penetrating disease phenotype, and/or after re-resection(s) are at increased risk of POR. This study aimed to assess POR after treatment of patients according to a clinical management algorithm incorporating these clinical risk factors.

Aims & Methods: In this multicenter prospective cohort study, CD patient (≥ 16 years) undergoing ileocolonic resection (ICR) in 14 hospitals were included from June 2017 until time of writing. The algorithm recommends endoscopy-guided pharmacological treatment in population 1 (low risk), i.e. absence of risk factors; in population 2 (high-risk), start of prophylactic prescription of thiopurines or anti-TNF within 8 weeks after ileocolonic resection. High risk is defined as presence of one or more above-mentioned clinical risk factors. Exclusion criteria included incomplete resection of macroscopic inflammation, absence of preoperative ileal disease, malignancy. According to the algorithm, endoscopy is performed at 6 months postoperatively. The endpoints are clinical recurrence (defined as HBI score > 7 or symptoms necessitating the start or switch of IBD medication for symptoms) and endoscopic recurrence (defined as Rutgeerts score ≥ 2 at endoscopy performed within 12 months after ICR, or intestinal inflammation necessitating start or switch of IBD medication).

Results: A total of 120 patients have been included in this study up to writing (48 (40%) male, median age at ICR 34.4 [IQR 25.4-51.5] years ICR was performed for strictures in 64 (55.7%) patients, and penetrating disease in 14 (15.7%) patients. The low risk population comprised 51 patients (43.2%) and the high risk population 67 patients (56.8%). In the low risk population, 69.8% (n=30) received no prophylaxis (in accordance with

algorithm). In the high-risk group at 6 months follow-up (n=54), 48.1% (n=26) received prophylaxis (in accordance with the algorithm), q.e. 28 (51.9%) high risk patients did not receive prophylaxis. Previous ileocolonic resection as risk factor was disregarded as a risk factor (n=13) most often, followed by penetrating disease (n=14) and smoking (n=9). Main reason to deviate from the treatment algorithm were patient's wish (high-risk n=9 (40%), low risk n=0). At the time of writing, 98 patients have reached the 6 months follow-up visit. Clinical recurrence at 6 months did not vary between high (n=7 (13.7%)) and low risk patients (n=14 (20.9%), $p=0.313$). Colonoscopy at 6 months was performed in 83/98 patients (84.7%), and showed endoscopic recurrence in 21 (52.5%) low risk patients and 28 (65.1%) high risk patients. Endoscopic recurrence rate in the low risk population was 53.3 % (n=16/30) in patients who were not treated with prophylaxis (in accordance with the algorithm) versus 38.5% (n=5/13) in patients treated with prophylaxis ($p=0.371$). In high risk patients treated with postoperative prophylaxis (in accordance with the algorithm) endoscopic recurrence rate was 38.5% (n=10/26) versus 64% (n=18/28) in patients in whom prophylaxis was not prescribed ($p=0.015$).

Conclusion: Adherence to a simple decision tool for the use of postoperative prophylaxis after ICR is only 50% in patients with clinical risk factors for POR. With regard to scheduled postoperative endoscopy at 6 months adherence is high. The rate of endoscopic POR when neglecting the clinical risk stratification for prophylaxis in patients with clinical risk factors is increased.

Disclosure: Nothing to disclose

P0628

LOCAL APPLICATION OF AUTOLOGOUS PLATELET-RICH PLASMA IS SAFE AND EFFECTIVE IN TREATMENT OF COMPLEX CROHN'S PERIANAL FISTULAE - RESULTS FROM SINGLE CENTER PILOT STUDY

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Introduction: Complex Crohn's perianal fistula (pCD) is a difficult-to-treat condition mainly due to the fact that its pathogenesis is not fully understood. Failure of wound repair and dysregulated inflammation are considered to play a key role in the persistence of the fistula tract. Current therapeutic strategies aiming at these pathogenetic pathways are effective in only up to 50% of patients. Novel therapies are therefore needed. Few preliminary reports suggest that autologous platelet-rich plasma (PRP) can enhance wound repair and may be effective in treating pCD, but conclusive results are lacking.

Aims & Methods: The aim of this study was to determine the efficacy and safety of autologous PRP in the treatment of pCD. A prospective, uncontrolled, single center study in a referral IBD center was conducted between July 2018 and February 2020. Adult Crohn's disease patients with pCD failing on antibiotics, immune suppression and/or biologics were eligible for the study.

All patients had non-cutting setons for a minimal period of 6 weeks prior study intervention. Autologous PRP was separated by centrifugation of 60 ml of peripheral blood in Harvest SmartPrep® System at the time of opera-

tion. After removing of seton(s), internal openings were closed by PDS 2/0 single suture and PRP was injected close to internal openings and fistula tracts. Patients were examined at outpatient clinic at week 1, month 1, 3 and 6 and any suspected side-effects of the treatment were noted. Treatment effect was assessed by perianal Crohn Disease Activity Index (PCDAI) assessed at baseline, month 1, 3, 6) and van Assche MRI score (assessed at baseline and month 6). The primary end-point was complete healing at month 6 defined as closure of all external fistula openings and absence of abscess on MRI.

Results: During the inclusion period, 21 patients (pts) with pCD were included (mean age 37 years, range 21-61; 11 men). The majority of pts were using antiTNF biologics (9 adalimumab, 7 infliximab), 2 pts were treated by ustekinumab, one by vedolizumab, two patients were on immunomodulators monotherapy.

The treatment was well-tolerated, the only side effects were minor local pain at the injection site and perianal soiling during maximum of seven days following intervention.

By May 2020, 19 patients finished the 6 months follow-up. Out of these 19 pts, fifteen (79%) reached the primary end-point of complete healing. Baseline PCDAI (median 5, range 2-9) decreased significantly as early as at month 1 (median 1, range 0-5; $p<0.001$) and remained further stable over 6 months. Van Assche MRI score decreased significantly from median of 13 (range 8-20) at baseline to 10 (range 4-18) at month 6 ($p<0.001$).

Conclusion: Local application of autologous platelet-rich plasma is safe and effective in inducing complete healing of difficult-to-treat complex Crohn's perianal fistulae.

Disclosure: Nothing to disclose

P0629

IMPACT ON QUALITY OF LIFE OF SETON PLACING IN PERIANAL CROHN'S DISEASE

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Introduction: Staged fistulotomy with a seton is considered to decrease the high incidence of continence disorders after surgical incision of a sporadic anal fistula [1]. Currently, in perineal Crohn's disease (CD) it is placed to guarantee a constant drainage and prevent septic complication while biologic therapy is ongoing [2].

Aims & Methods: This study aimed to assess the impact of seton placing on long-term quality of life after surgery for perineal CD. Data of 66 consecutive CD patients operated on from 2014 to 2019 for perianal fistula or abscess were retrieved. Thirty-four of them had a seton placed during surgery and they kept it on while they had anti-TNF-alpha therapy. Patients were interviewed with the Cleveland Global Quality of Life (CGQL) and SF-12 quality of life questionnaires. Disease activity was defined as Harvey-Bradshaw Index (HBI) and Perianal Disease Activity Index (PDAI). Comparisons between groups were carried out with non-parametric tests multiple regression models were used to assess predictors of quality of life.

Results: The total CGQL score and SF-12 mental component score (MCS) were significantly higher (and thus better) in the seton group than in patients treated without seton ($p=0.03$ and $p=0.02$, respectively). On the contrary, SF-12 physical component score (PCS) was not different between the two groups. HBI was significantly lower in patients in the seton group ($p=0.01$). At multivariate analysis, seton placement and HBI confirmed to be independent predictors of long-term SF-12 mental component score (MCS) while only HBI confirmed to be a predictor of total CGQL score.

Conclusion: Seton placing during anti-TNF-alpha therapy is independent-ly associated to a better MCS. Unexpectedly, this device, instead to cause a psychological distress, seem to assure patients during their biologic therapy providing psychological benefit beyond the mere medical effect.

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Disclosure: Nothing to disclose

P0630

INCIDENCE AND RISK FACTORS ASSOCIATED WITH RECURRENCE OF CROHN'S DISEASE AFTER DEFINITIVE PANPROCTOCOLECTOMY AND ILEOSTOMY: THE IFARPI STUDY

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Introduction: Total proctocolectomy with definitive ileostomy (TPC-DI) may be the latest therapeutic option for patients with extensive colonic or severe perianal Crohn's disease (CD) refractory to medical therapy. How-

ever, the rate of small bowel recurrence after TPC-DI for CD varies between different series and depends on whether clinical or surgical recurrence is assessed. Moreover, the predictors of recurrence in these patients are not clearly defined.

Aims & Methods: We made a retrospective multicentric cohort study. Patients with TPC-DI for indeterminate colitis or ulcerative colitis, or patients with an oversewn rectal stump were excluded.

CD clinical recurrence was defined as suggestive symptoms combined with compatible endoscopic and/or radiological findings, after other causes were excluded. CD surgical recurrence was defined as need of re-surgery for clinical recurrence. Characteristics of the study population at the time of TPC-ID were evaluated as risk factors potentially associated with recurrence.

Results: Nineteen Spanish tertiary hospitals participated in the study which included 174 CD patients who underwent TPC-DI from June 1967 to March 2019 and who had been followed-up after surgery. We included 60 patients (34.5%) who underwent TPC-DI in the pre-biological era and 114 (65.5%) in the biological era. Median follow-up time after TPC-DI was 11 years (IQR 4-21).

Male/female (%); Age-median (IQR); Disease duration until TPC-ID-median (IQR)	94/80 (54/46); 53 (42-63); 7.5 (2-15)
Age at diagnosis according to Montreal classification-n (%): A1, A2, A3; Disease location-n (%): Colonic, Ileocolonic, Perianal; Disease phenotype according to Montreal classification-n (%): Non stricturing-non-penetrating, Stricturing, Penetrating	20 (11), 128 (74), 26 (15); 81 (47), 93 (53), 93 (53); 76 (44), 28 (16), 70 (40)
Smoking habits-n (%): Smokers, Non-smokers	68 (39), 106 (61)
Patients with previous surgical procedures-n (%): Surgeries for patient before TPC-DI-n (%): ≤2, ≥3-5; Type of surgery before TPC-DI-n: Ileocolonic resection, Segmental colonic resection, Colostomy, Small bowel resection, Anal surgery	96 (55); 69 (72), 31 (28); 75, 67, 12, 3, 52
Patients with medication before TPC-DI-n (%): Corticosteroids, Immunosuppressants, Anti-TNF, Vedolizumab, Ustekinumab,	149 (86), 115 (66), 85 (49), 12 (7), 6 (3)
Number of biologics before TPC-DI-n (%): ≥1, ≥2, ≥3	40 (47), 37 (44), 8 (9)
Indication for TCP-DI-n (%): Acute complication (toxic megacolon, massive hemorrhage or perforation), Refractory luminal disease, Colonic dysplasia	18 (10), 149 (86), 7 (4)

[Characteristics of the study population (n = 174 patients) at the time of TPC-ID]

Of the 130 patients in whom activity was assessed at the ileal level in the surgical specimen, 77 (60%) had macroscopic and/or microscopic activity. One third of patients (33%) received recurrence prophylaxis after surgery. The clinical and surgical recurrence were 29.9% (52 patients) (95% CI, 23.5-37.2) and 11.5% (95% CI, 7.5-17.2), respectively. The median time to clinical recurrence time was 8.5 years (IQR 3-13).

The incidence rate of clinical recurrence was 2.6 per 100 patients/year, and the surgical recurrence was 1 per 100 patients/year.

The cumulative incidence rate of clinical recurrence over time was as follows: 2% at 1 year, 11% at 5 years, 20% at 10 years, 33% at 15 years, and 37% at 20 years of follow-up. The cumulative incidence rate of surgical recurrence over time was as follows: 0% at 1 year, 2% at 5 years, 6% at 10 years, 18% at 15 years and 20% at 20 years of follow-up.

The factors associated with a higher risk of clinical recurrence were: ileocolonic location (HR 2.07; 95% CI 1.13 - 3.78, $p=0.0135$) and histological activity in ileum (HR 2.59; 95% CI 1.19 - 5.65, $p=0.0093$). There was an association between stricturing-penetrating phenotype, perianal involvement, fewer years of evolution since diagnosis and clinical recurrence but did not reach statistical significance.

Conclusion: Small bowel recurrence after TPC-DI for CD is not uncommon. In our serie, which includes a large number of patients treated in the biological era, the risk of clinical recurrence was higher in patients with history of ileal disease or with histological activity in ileum in the surgical

specimen. In this subgroup of patients, continued medical therapy, or at least continued objective surveillance (endoscopic and/or radiological), may be advisable in order to identify asymptomatic disease recurrence, guide therapy and avoid new surgeries.

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P0631

THE INFLUENCE OF PREOPERATIVE MEDICATIONS IN SURGICAL COMPLICATIONS IN INFLAMMATORY BOWEL DISEASE IN SPAIN: A MULTICENTER STUDY OF GETECCU

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Introduction: It has been suggested that biologic therapy may increase the risk of postoperative complications in inflammatory bowel disease (IBD), but the evidence is scarce. Our aim was to evaluate whether the treatment with anti-TNF agents, ustekinumab and vedolizumab increase the risk of complications after surgery in IBD patients.

Aims & Methods: IBD patients undergoing intra-abdominal surgeries between 1st January 2009 and 31st December of 2019 were retrospectively included. Data collection included clinical characteristic of the disease, biochemical parameters and surgery aspects. Postsurgical complications were defined as those occurring within 30 days after surgery. IBD surgeries were classified according to the presence or absence of postsurgical complications. Biologic exposure was considered when the last dose of anti-TNF, ustekinumab or vedolizumab was received 3 months prior to surgery. Both groups were compared according to the clinical characteristics and the pre-operative therapy received. Predictive factors of postsurgical complications were identified by logistic regression analysis.

Results: A total of 1,443 surgeries carried-out in 1,319 patients were included. Surgery for Crohn's disease (CD) was performed in 82% of cases, for ulcerative colitis (UC) in 17% and for unclassified-IBD (U-IBD) in 1.2%. Anti-TNF therapy previous to surgery was administered to 359 patients, vedolizumab to 53 patients and ustekinumab to 63 patients. 18% of the patients were operated on emergency and 82% on elective surgery. The group with preoperative biological therapy required more corticosteroids, more blood transfusions and more intravenous iron before surgery

compared to the group without it. CD was more prevalent in the group without biologic therapy than in that receiving this treatment (58% vs 25%). Postoperative complications were reported, overall, in 36% of the cases (N=527), including dehiscence, infection, obstruction, ileus, bleeding, thrombosis, fistula and evisceration. 12% of the patients needed to be re-operated in the postoperative period due to complications. Hospital admission after the discharge was necessary in 7.4% of the patients. The need of previous blood transfusion, being male and emergency surgery were factors associated with the development of postsurgical complications in the multivariate analysis, while ileal location was negatively associated (table 1). Postoperative complications were reported in 38% (n=136) of patients under anti-TNF therapy, in 40% (n=25) in the ustekinumab group, in 43% (n=23) in the vedolizumab group, and in 24% (n=350) in the group without biological therapy. Preoperative biological treatment was not associated with a higher risk of postsurgical complications in the multivariate analysis.

	Odds Ratio	95% confidence interval	P value
Male gender	1.63	1.27-0.90	0.001
Previous blood transfusion	2.64	1.63-4.27	0.001
Ileal location (CD)	0.64	0.5-0.82	0.001
Emergency surgery	1.46	1.07-1.99	0.018

[Table 1. Risk factors of postoperative complications in the multivariate analysis.]

Conclusion: Biological therapy at any given moment throughout the preoperative period was not associated with postsurgical complications in IBD. No differences in postoperative complications were observed between anti-TNF treatment, ustekinumab and vedolizumab.

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P0632 LONG-TERM EFFECTIVENESS OF DARVADSTROCEL IN PATIENTS WITH COMPLEX PERIANAL FISTULAS IN CROHN'S DISEASE: RESULTS FROM INSPECT, A RETROSPECTIVE CHART REVIEW STUDY IN EUROPE

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Introduction: Darvadstrocel (DVS), a suspension of expanded allogeneic adipose-derived mesenchymal stem cells, was demonstrated to be an effective and safe treatment for complex perianal fistulas (CPAF) in patients with Crohn's disease (CD) who didn't respond to conventional/biological treatments, or both, up to 52 weeks (w), as shown in the randomised, double-blind, ADMIRE-CD trial.^{1,2} There is a need for establishing the long-term effectiveness of DVS, the one-time minimally invasive treatment for CPAF.

Aims & Methods: Aims of this study were to evaluate the longer-term effectiveness and safety of DVS (vs control) in patients enrolled in the ADMIRE-CD trial. INSPECT, a multi-centre, retrospective chart review study across eight countries in Europe, aimed to collect +2 years of real-world data for patients enrolled in ADMIRE-CD. Charts were abstracted from the ADMIRE-CD investigational sites for patients who completed ≥52w follow-up in the trial and accepted to participate in this study. Index was defined as DVS or placebo administration at ADMIRE-CD initiation. Evaluated outcomes included clinical remission, sustained remission, time to relapse (among those in remission at 52w) and adverse events of special interest (AESIs; tumourigenicity and ectopic tissue formation). Time to first relapse was estimated using the Kaplan-Meier method with p-values derived using Cox proportional hazards model.

Results: 89/131 patients who completed ≥52w in ADMIRE-CD consented to participate (43 DVS; 46 control) in INSPECT across 35/49 ADMIRE-CD sites. Key characteristics at index are presented in Table 1. At index, INSPECT patients (n=89) were comparable to patients who completed ≥52w in ADMIRE-CD but 'not included' in INSPECT (n=42) in age, gender, disease duration, and mean CD activity index (data not shown), except for anti-TNF use (with/without immunosuppressants): 72.0% vs 38.1% in included vs non-included patients, respectively (p< 0.05). At 52w, 59.6% (n=53/89)

and 64.3% (n=27/42) were in clinical remission in included vs non-included patients, respectively. In this study, clinical remission observed in DVS and control groups at 52w post-index date: 67.4% (n=29/43) vs 52.2% (n=24/46); 104w post-index date: 53.5% (n=23/43) vs 43.5% (n=20/46); and 156w post-index date: 53.5% (n=23/43) vs 45.7% (n=21/46), respectively. No significant differences were observed between groups for time to first relapse of ADMIRE-CD treated fistula. One AESI in each group (DVS: benign tumor not product related and control: malignant tumor) was reported during the study period.

Conclusion: This is the first study examining the longer-term effectiveness and safety of DVS, which demonstrated that >50% of patients were able to sustain the remission status up to 3 years post-DVS administration.

	DVS (n=43)	Control (n=46)	P-Value
Characteristics at index*			
CD disease duration, years, mean (SD)	12.7 (11.1)	11.0 (8.4)	0.42
Multiple tract fistula, n (%)	23 (53.5)	17 (37.0)	0.12
Concomitant anti-TNFs (with/without immunosuppressants), n (%)	33 (76.7)	31 (67.4)	0.33
Clinical outcomes post-index			
Clinical remission at 52 weeks, n (%) [†]	29 (67.4)	24 (52.2)	0.14
Clinical remission at 104 weeks, n (%) ^{†‡}	23 (53.5)	20 (43.5)	0.35
Clinical remission at 156 weeks, n (%) [†]	23 (53.5)	21 (45.7)	0.46
Clinical outcomes of patients in clinical remission[†] at 52 weeks post-index			
Sustained clinical remission at 104 weeks, n/N (%) [§]	19/29 (65.5)	17/24 (70.8)	0.68
Sustained clinical remission at 156 weeks, n/N (%) [§]	16/29 (55.2)	13/24 (54.2)	0.94
Clinical progression in patients who only completed 52 weeks of ADMIRE-CD			
Relapse by 104 weeks, n/N (%)	7/17 (41.2)	5/18 (27.8)	0.49
Relapse by 156 weeks, n/N (%)	7/17 (41.2)	7/18 (38.9)	0.89
≥1 surgical intervention by 156 weeks, n/N (%)	1/17 (5.9)	3/18 (16.7)	0.60

*Data from ADMIRE-CD trial. [†]Clinical remission was defined as closure of all external fistula openings that were draining at baseline, confirmed by clinical assessment or medical record documentation of remission/complete response. [‡]Includes data from INSPECT and ADMIRE CD trial (for those who were in the trial for 104 weeks). [§]Sustained clinical remission was defined as patients remaining in clinical remission at follow-up visits who were in remission at 52 weeks. Unadjusted p-values are from student's t-test for continuous outcomes or chi-squared tests for binary and nominal outcomes (or Fisher exact test if there are ≤5 patients in a comparison category).

[Table 1: Characteristics at index and clinical outcomes in DVS and control group: INSPECT study results]

References: 1. Panés J, et al. Lancet 2016;388:1281-90. 2. Panés J, et al. Gastroenterology 2018;154:1334-42.

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TIME TRENDS FOR POSTOPERATIVE RECURRENCE AFTER ILEOCECAL RESECTION IN CROHN'S DISEASE: DETAILED EVALUATION OF ASSOCIATED FACTORS

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Introduction: The rate of ileocecal resection (ICR) in Crohn's disease (CD) has decreased over the past decades. In this study we aimed to explore the time trends of postoperative recurrence (POR) after primary ICR, as well as the congruity and correlation between POR and the following factors:

1. preoperative factors: timing of ICR after CD diagnosis, indications for ICR, preoperative exposure to CD medication,
2. Peroperative factor: surgical technique, and;
3. postoperative factors: endoscopy within 18 months and prophylactic medication.

Aims & Methods: In this multicenter retrospective cohort study, CD patients undergoing primary ICR between 2000 and 2019 in 10 hospitals were included. Four time periods were analyzed: 2000-2004, 2005-2009, 2010-2014 and 2015-2019. Time trends were evaluated with Kaplan-Meier survival. The endpoints were clinical recurrence (start or switch of corticosteroids, immunomodulators (IM) or biologics for clinical complaints), endoscopic recurrence (Rutgeerts score $\geq 2b$ at endoscopy performed within 18 months) and surgical recurrence (re-resection).

Results: 839 patients were included in this study (326 (39%) male, median age at ICR 32.2 years [IQR 24.0 - 45.1], median follow-up 5.9 years [IQR 2.5 - 10.6]). Over the study period, the rate of clinical ($p=.008$) and endoscopic recurrence ($p<.001$) increased significantly, whereas no significant change in the rate of surgical recurrence was observed ($p=.075$). Clinical POR within 2 years occurred in 36 (27.6%) patients in '00-04, 66 (33.7%) in '05-09, 117 (46.7%) in '10-14 and 117 (46.5%) in '15-19. Endoscopic POR occurred in 9 (6.9%) patients in '00-04, 29 (14.8%) in '05-09, 62 (24.9%) in '10-14 and 94 (31.7%) in '15-19. Surgical recurrence within 3 years occurred in 4.6% of patients, 7.2%, 7.2% and 8.3 % during consecutive time periods. The median interval between CD diagnosis and ICR was 3.1 years [IQR 0.7-8.3] and did not differ between time periods ($p=0.349$). Age at time of ICR, gender and smoking did not differ significantly between time periods. Stricturing CD was the most common indication for ICR in all time periods and remained stable over recent years ('00-04: 58.9%, '05-09: 45.2%, '10-14: 42.6%, '15-19: 48.6%), the frequency of refractory disease

or as step-up therapy as indication for ICR fluctuates over the study period ('00-04: 15.9%, '05-09: 22.1%, '10-14: 32.7%, '15-19: 28.8%), whereas the frequency of penetrating disease decreased during recent years ('00-04: 22.7%, '05-09: 27.1%, '10-14: 21.6%, '15-19: 19.8%). Preoperative use of IM (MTX and/or thiopurine) and biologics (anti-TNF therapy, vedolizumab, ustekinumab) increased, as well as laparoscopic approach (27.8% in '00-'04 vs 73.0% in '15-'19), postoperative endoscopy within 18 months ($p=.000$) and postoperative prophylactic medication.

	2000-2004	2005-2009	2010-2014	2015-2019	P
Preoperative anti-TNF use (%)	7 (5.3)	49 (24.6)	151 (60.2)	164 (63.8)	0.000
Preoperative immunomodulator use (%)	50 (37.9)	121 (60.8)	187 (74.5)	191 (74.3)	0.000
Postoperative prophylaxis MTX(%)	0	5 (2.5)	9 (3.5)	9 (3.5)	0.001
ADA (%)	0	7 (3.5)	30 (11.9)	28 (10.9)	
IFX (%)	2 (0.2)	5 (2.5)	15 (6.0)	26 (10.1)	
UST (%)	0	0	0	3 (11.7)	

[Preoperative medication and postoperative prophylactic medication after ICR in CD patients]

Conclusion: From 2000 to 2019, the risk of clinical and endoscopic POR after primary ICR in CD increased, whereas the risk of surgical recurrence was stable within this cohort. These findings might be explained by changed indications for ICR, increased exposure to IM and biologics preoperatively, a marked increase in laparoscopic ICRs, as well as postoperative factors of increased CD medication use (both prophylaxis and for symptoms) and performance of endoscopies.

Disclosure: Nothing to disclose

P0634

LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION STRATEGY FOR LARGE SUPERFICIAL NEOPLASMS IN INFLAMMATORY BOWEL DISEASES

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Introduction: Patients with long-standing active inflammatory bowel diseases (IBD) have an increased risk of colorectal dysplasia. Efficacy of endoscopic resection has been demonstrated for small polypoid neoplasms providing that it is en bloc and complete. Feasibility of endoscopic submucosal dissection (ESD) for large neoplasms has been shown in small series but no long-term data are available.

Aims & Methods: **Aim:** to evaluate clinical outcomes of ESD for large IBD colorectal superficial neoplasms. Prospective case series of consecutive large (≥ 20 mm) superficial neoplasms within the colitic IBD mucosa referred for ESD. All patients had a long-standing ulcerative colitis in clinical remission. Short-term (en bloc and R0 resection rates) and long-term outcomes (residual and metachronous cancer rates within a minimum

24-month follow-up) were evaluated. Neoplasms were characterized by white light endoscopy and chromoscopy with narrow band imaging and acetic acid.

Results: Thirteen patients with 15 superficial neoplasms underwent ESD. Neoplasm features: median size 28 mm (range 20-50 mm), nonpolypoid morphology in 14 (93%) (LST-NG in 4), scar presence in 6 (40%), location rectum and left colon in 9 (60%). Margins were better delineated with acetic acid in 7 (47%). En bloc and R0 resections rates were 87% (n.13: 2 cases underwent piecemeal EMR due to TEM scar) and 80% (n.12), respectively. Resection was curative in all cases (T1a low-risk cancer was diagnosed in 1 case in the perineal rectum). Submucosal fibrosis was observed in 9 (60%). No adverse events occurred. Median follow-up was 44 months (range 24-54): minute adenomatous residues were detected in the 2 (13%) EPMR cases. Metachronous neoplasms were identified in 5 (33%): 4 underwent endoscopic resection, 1 underwent proctocolectomy due to multiple superficial neoplasms with indistinct margins adjacent to the ESD scar.

Conclusion: ESD for IBD neoplasms is feasible and effective, although the difficulty gradient is high due to high prevalence of LST-NG, scars, and SM fibrosis. ESD may avoid surgery but a strict surveillance is mandatory for a high incidence of metachronous lesions.

Disclosure: Nothing to disclose

P0635

POSTOPERATIVE PROPHYLACTIC THIOPURINES OR BIOLOGICALS ARE PROTECTIVE FOR CLINICAL AND ENDOSCOPIC RECURRENCE AT SHORT TERM FOLLOW-UP AFTER PRIMARY ILEOCECAL RESECTION IN CROHN'S DISEASE, BUT NOT ASSOCIATED WITH A LONG-TERM BENEFICIAL EFFECT ON THE RISK OF RE-RESECTION

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Introduction: The prediction of the postoperative disease course after ileocecal resection in Crohn's disease (CD) patients remains challenging. Available data often concern small cohorts and mixed populations of primary ileocecal resection (ICR), and ileocolonic re-resections. This study aims to identify clinical risk factors for postoperative clinical, endoscopic and surgical recurrence in CD patients after primary ileocecal resection

Aims & Methods: In this multicenter retrospective cohort study in 10 hospitals, CD patients who underwent primary ICR between 2000 and 2019 were identified. The endpoints included: Clinical recurrence (defined as

the start or switch of IBD medication for symptoms), endoscopic recurrence (defined as Rutgeerts score $\geq 2b$ within 18 months after ICR) and surgical recurrence (re-resection). The following factors were included in a backward selection multivariable Cox regression analysis: Sex, age, Montreal classification, smoking status, preoperative biological use, thiopurine use, perianal fistula, time between diagnosis and ICR, length of resected segment in cm, surgical approach and prophylactic medication with biological or thiopurine.

Results: The total cohort comprised 839 patients (326 [39%] male, median age at ICR 32.2 years [IQR 24.0 - 45.1]. Median total follow-up time after ICR was 5.9 years (IQR 2.5 - 10.6). In total, 271 patients (32%) were active smokers. ICR was performed for strictures in 401 (48%) patients and penetrating disease in 188 (22%). Postoperatively, 442(53%) patients received no prophylaxis, 91 (11%) 5ASA, 174(21%) thiopurines, 71 (9%) anti-TNF monotherapy, 8 (1%) other biologic therapy and 41(5%) anti-TNF and thiopurine combination therapy. Postoperative clinical recurrence was observed in 514 (61%) patients after a median of 15.7 months (IQR 7.4 - 42.7). Active smoking (HR 1.3 [95%CI 1.1 - 1.6]) and biological use prior to ICR (HR 1.6 [95%CI 1.3 - 1.9]) were associated with postoperative clinical recurrence. Penetrating disease behaviour (HR 0.8 [95%CI 0.6-0.9]) and prophylactic postoperative medication (HR 0.6 [95%CI 0.5 - 0.7]) were protective factors for clinical recurrence. Endoscopic recurrence within 18 months after ICR was observed in 171 (21%) patients. Biological use prior to surgery (HR 1.7 [IQR 1.2-2.3]) was associated with endoscopic recurrence. Stricturing disease behaviour (B2 versus B1 HR 0.6 [IQR 0.4-0.8]), penetrating disease behaviour (B3 versus B1 HR 0.5 [95%CI 0.3 - 0.7]) and postoperative prophylaxis (HR 0.4 [95%CI 0.3 - 0.6]) were protective factors for postoperative endoscopic recurrence within 18 months. Surgical recurrence was observed in 143 (17%) patients within a median 4.4 years (IQR 1.8 - 7.8). Active smoking (HR 1.8 [95%CI 1.2 - 2.6]), biological use prior to ICR (HR 1.8 [95%CI 1.2 - 2.6]) and ileocolonic disease localisation (L3 versus L1 HR 1.5 [95%CI 1.0 - 2.1]) were significant risk factors for re-resection. Postoperative prophylaxis was not a significant protective factor for surgical recurrence.

Conclusion: Biological use prior to surgery is a significant risk factor for clinical, endoscopic and surgical recurrence after primary ICR. In contrast to current guidelines, penetrating disease behaviour seems associated with lower risk of clinical and endoscopic recurrence. Postoperative prophylactic medication is protective for clinical and endoscopic recurrence at short term follow-up; however, a beneficial long-term effect on the risk of re-resection has not been demonstrated.

Disclosure: Nothing to disclose

P0636

POST-OPERATIVE COURSE OF CROHN'S DISEASE AFTER ILEOCAECAL RESECTION: RESULTS OF A RETROSPECTIVE MONOCENTRIC COHORT STUDY

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Introduction: More than 50% of Crohn's disease (CD) patients require an ileocaecal resection during the course of their disease. The objectives of this study were to describe the current post-operative course after an ileocaecal resection, to identify risk factors for recurrence and to evaluate the impact of post-operative available therapies on clinical and endoscopic recurrences.

Aims & Methods: In this retrospective monocentric study, all CD patients undergoing an ileocaecal resection between 2009 and 2018 in Lyon Sud university hospital were included. During follow up, we analysed all medical records on postoperative clinical recurrence (CR) (HBI > 4), endoscopic recurrence (ER) (Rutgeerts score > i1) and CD-related treatments.

Results: Eighty-eight patients were included, with a median follow up of 4.38 years. The cumulative postoperative CR and ER rates were 35% and 70%, respectively, with 45% of CR and 80% of ER among the total of recurrences occurring during the first post-operative year. Actuarial analysis of symptom free survival showed a median survival of 8.8 years for patients graded i0-i1, and of 4.2 years for patients graded i2-i4 at 1 year after surgery. In multivariate analysis, smoking (OR 3.63 ; IC95% [1.04;12.73], p=0.043) and histological margins ≤ 2 cm (OR 6.27 ; 95%CI [1.93;2.;35], p=0.002) were independent risk factors for ER at 6 months after surgery. Stricturing behaviour (OR 4.25 ; IC95% [1.25;14.42], p=0.020) and ER within the first year after surgery (OR 7.92 ; IC95% [2.15;29.07], p=0.002) were independent risk factors for clinical recurrence. In patients with postoperative ER, administration of anti-TNFα or ustekinumab was associated with further improvement of endoscopic severity in 60.8% and 72.7% of cases, respectively, and 34.7% and 54.5% of patients achieved endoscopic remission.

Conclusion: This study confirms a pejorative long-term disease outcome in patients with ER during the first post-operative year. Histological margins represent a risk factor for ER requiring the prophylaxis to be adjusted. The treatment of postoperative ER has proven effective in improving endoscopic severity and prevent further clinical recurrences.

Disclosure: Nothing to disclose

Poster presentations

Other lower GI disorders

Poster Presentations

Other lower GI disorders

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Other lower GI disorders

09:00-19:00 / Poster Exhibition

P0637

LONG-TERM REMISSION IN A PATIENT WITH EOSINOPHILIC COLITIS (EC) AFTER DETECTION OF LOCAL FOOD ANTIGEN-SPECIFIC IGE AND SUBSEQUENT ALLERGEN AVOIDANCE

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Introduction: Eosinophilic gastrointestinal disorders (EGIDs) are a heterogeneous group of rare conditions, characterized by eosinophilic infiltration (EoIn) of the gastrointestinal mucosa, rarely the muscularis or tunica serosa, in connection with GI-symptoms. Other causes of EoIn must be excluded before EGID is diagnosed. EGIDs present as eosinophilic gastritis, eosinophilic gastroenteritis and EC. An immune pathogenesis seems to be involved, but the causal triggers are unknown.

Aims & Methods: Here we report an a 48yr old male suffering from chronic diarrhea and recurrent IBS symptomatology (IBS-S 266). Comprehensive serological and differential diagnostic tests could not reveal the cause of the diarrhea. Histology of the lower GIT showed an unspecific colitis and increased EoIn-score, but no explanation for the EC could be found. Thus, an endoscopically controlled segmental intestinal lavage was performed to search for local IgE antibodies.

Results: Lavage fluid show elevated levels of eosinophilic cationic protein and increased specific IgE towards wheat, corn, and borderline IgE-titers towards nuts, pork and beef, while cutaneous or serological test were inconclusive. Subsequent allergen avoidance and antiallergic treatment resulted in complete clinical and histological remission of EC (IBS-S 46). After two years follow-up the patient was free of diarrhea, no significant IgE titers were detected and tissue eosinophilia was absent.

Conclusion: Although the exact triggers for EC are yet unknown, this case illustrates that local food-IgE may be related to the manifestation of an EGID. Local eosinophil activation, IgE-antibodies and clinical symptoms were reduced after specific allergen avoidance. Thus, intense efforts should be made to clarify potential triggers for EC like drugs, salizylate hypersensitivity, but also food antigens. This case shows that the EC diagnosed initially should be re-classified as a local seronegative GI-allergy, as a possible secondary cause for an EGID.

Disclosure: Nothing to disclose

P0638

FROZEN FECAL MICROBIOTA TRANSPLANTATION FOR PATIENTS WITH STEROID RESISTANT GASTROINTESTINAL GRAFT-VERSUS-HOST DISEASE

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Introduction: Given the association between acute graft-versus-host-disease (GVHD) undergoing allogeneic hematopoietic stem cell transplantation (allo-HCT) and the gut microbiota, fecal microbiota transplantation (FMT) has been evaluated as an alternative treatment option. However, the evidence to support the effectiveness of FMT in treating GVHD is very limited, and FMT carries the risk of infection transmission.

Aims & Methods: The aim of this pilot study was to evaluate the effectiveness and safety of frozen FMT for the treatment of acute GVHD. A total of 4 patients with steroid refractory gastrointestinal (GI) acute GVHD underwent frozen FMT via upper endoscopy or colonoscopy from unrelated, healthy donors. Complete response (CR) was defined as resolution of GI symptoms or reduction of steroid dose to 5 mg of prednisone. Clinical improvement was defined as a decrease of stool volume < 500 mL and bleeding relieved.

Results: Patients received a range of 1-4 FMT courses. The detailed patient data are summarized in Table 1. Frozen FMT was well tolerated. Three patients had partial improvement, and 1 patient no response. Patient #1 developed *Klebsiella pneumoniae* bacteremia 4 days after 1st FMT, and extended-spectrum beta-lactamases (ESBL) producing *Escherichia coli* (*E. coli*) bacteremia 3 days after 2nd FMT. Patient #4 developed ESBL (-) *E. coli* bacteremia 5 days after 1st FMT. These infectious events could not be directly related to FMT because pathogenic bacteria were not detected in FMT inoculum. Three patients died from consequences of active GVHD, while one patient was free of GVHD after treatment with ruxolitinib.

Conclusion: FMT could serve as a therapeutic option for acute GI GVHD. However, its effectiveness and safety need further investigation. In addition, caution for possible complication should be exerted in highly immunocompromised patients, since antibiotics should be withheld to allow for persistent microbiota engraftment.

Disclosure: Nothing to disclose

P0639

GUT MUCOSA DISSOCIATION PROTOCOLS IMPACTS SINGLE CELL MRNA SEQUENCING RESULTS

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Introduction: Single cell mRNA sequencing (scRNAseq) is changing the way we look at biology. It has identified novel cell types in the gut and has elucidated their potential role in disease processes. Moreover, it has helped to clarify the role of specific cell types in the response to therapeutics. However, most single cell studies performed on gut mucosa from live individuals are limited in sample size (1,2,3). This is in part because fresh material is used, which is logistically demanding. This limits the number of samples per batch, inducing potential batch effects. An additional problem is that the outcomes of single cell studies may be affected by the method of tissue dissociation. For example, a two-step digestion protocol, such as the current gold standard protocol to dissociate gut mucosa, in which cell subsets are dissociated using different chemicals, possibly induces differences on the cellular level.

Aims & Methods: We developed a one-step digestion protocol which can be used to dissociate multiple samples simultaneously, using cryopreserved gut mucosal biopsies. We compared this protocol to the current gold standard protocol, and to a recently published protocol using an enzyme for cold digestion(5). We investigated viability, cell composition, gene expression and protocol efficiency to, using FACS data and mRNAseq data of 20.500 gut mucosal cells of 20 healthy individuals, generated using each of the three protocols.

Results: In flow-cytometry and single cell mRNA sequencing, we showed that our one-step digestion protocol provides good cell viability (70-80%) and cell composition comparable to the gold standard protocol (33% B cells, 16% T cells, 6% mesenchymal, 2% myeloid, 1% endothelium, 41% epithelium). The cold digestion protocol provided more epithelial cells (63%) and fewer mesenchymal cells (0.1%) than the other two protocols.

Conclusion: The dissociation protocol that we present here reduces work load and logistical challenges and enhances intestinal disease research. Furthermore, we find that the choice of dissociation protocol impacts scRNAseq results. In the design of studies, one should choose the dissociation protocol that provides adequate representation of the relevant cell types.

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Disclosure: Nothing to disclose

P0640

IMMUNE SYSTEM OF STUDENTS WITH REGULAR AND IRREGULAR BOWEL HABITS

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Introduction: Slowing down the circadian rhythm of the intestine is a risk factor for constipation, obesity and colorectal cancer, and also increases the risk of cardiovascular mortality by 21-39% [1-4]. However, the effect of a delayed bowel habits on the immune system remains poorly understood.

Aims & Methods: The aim of this work was to compare the immune system in individuals with regular circadian bowel rhythm in subjects with irregular bowel habits. We examined 74 medical students (age 21-29, 51 women and 23 men). The defecation rhythm was monitored: the weekly frequency and circadian acrophase of the stool rhythm were determined. There was a regular diurnal bowel rhythm (euenteria) with a frequency of defecation of at least 7 times a week and an irregular slow bowel rhythm (bradyenteria) with a frequency of defecation of 1 to 6 times a week. The level of satisfaction with nutrition and physical activity was studied. The activity of the immune system was determined by 10 main indicators. We assessed the risk of developing allergies, coughing, runny nose, dry skin, physical overload, weakness, nervousness, drowsiness, inattention, and insomnia on a 10-point scale. The normal level of activity of the immune system was considered 31 points, and reduced - more than 31 points. The normal level of quality of life was considered to be between 70% and 100% of the optimal level.

Results: Bradyenteria was diagnosed in 47% of the students, and euenteria - in 53%. In students with regular enteral rhythm (euenteria), morning acrophase of the stool rhythm occurred in 61% of cases, and its absence in 39% of cases. In students with delayed enteral activity (bradyenteria), morning acrophase of defecation occurred in 29% of cases, and the absence of morning acrophase of defecation occurred in 71% of cases. Consequently, the absence of morning acrophase of the stool rhythm increased the risk of bradyenteria by almost 2 times. Satisfactory nutrition with euenteria had 58% of students, while bradyenteria - 27%. Consequently, the nutritional satisfaction of students with bradyenteria was almost 2 times lower than that of students with euenteria. Normal physical activity in euenteria was in 47% of students, and in bradyenteria - in 33%. Consequently, students with bradyenteria were almost 1.4 times less satisfied with their physical activity than students with euenteria.

Students with bradyenteria were significantly less satisfied with their diet and physical activity than students with daily bowel habit. Normal levels of the immune system were found in 65% of students with euenteria, but only in 47% of students with bradyenteria. Reduced levels of the immune system in students with bradyenteria (53%) were more common than in students with euenteria (35%). Bradyenteria reduced the likelihood of a normal immune system level and increased the risk of a reduced immune system level by 18%.

The normal level of quality of life was detected in 88% of persons with euenteria, but only 47% of persons with bradyenteria. Consequently, bradyenteria increases the risk of reducing the normal level of quality of life by almost 2 times.

Conclusion: 1. Irregular bowel habits in the form of bradyenteria with a frequency of stools from 1 to 6 times a week is associated with dissatisfaction with nutrition and physical activity.

2. Irregular bowel habits contribute to lower levels of the immune system and lower quality of life.

3. The regular bowel habit is associated with a normal level of nutrition and physical activity, which contributes to a normal level of immune system.

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Disclosure: Nothing to disclose

P0641

COLORECTAL CANCER PROGNOSIS AND DIAGNOSIS UTILITY OF A NEW NON INVASIVE INFLAMMATORY BLOOD BIOMARKER

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Introduction: Systemic inflammation is associated with the development and progression of colorectal cancer (CRC). Blood analytical markers that reflect the inflammatory response like NLR (neutrophil(N)/lymphocyte(L) ratio), PLR (platelet(P)/L ratio) and SII or systemic inflammation index (P×N/L) have been proposed as non-invasive, potential tools for the prognosis of CRC

Aims & Methods: To investigate the differences of these analytical markers (NLR, PLR, SII and a new marker called NP/LHb based on the combination of N x P divided by L x Haemoglobin(Hb)) in healthy participants and CRC patients and also in CRC patients at the time of the diagnosis and 6 months before. Furthermore, to study the association between analytical markers and the TNM stage of the CRC and finally to analyze its usefulness in CRC diagnosis. We retrospectively recruited CRC patients diagnosed between 2010 and 2016 at Hospital Clínico Lozano Blesa and healthy participants who present a normal colonoscopy obtained from a registry of CRC population screening program. Demographic, tumor-related, and analytical variables were collected from CRC patients at 2 different times; at the time of cancer diagnosis and 6 months before. The same demographic and analytical variables were collected from the healthy participants from a blood test close to the screening colonoscopy. We calculated differences between groups of NLR, PLR, SII and NP/LHb and their sensitivity (Se), specificity (Sp), positive and negative predictive values (PPV, NPV) and area under the ROC curve (AUROC) for the diagnosis of CRC and tumor progression.

Results: 240 CRC cases (mean age=68.9±11.9, male=62.5%) and 219 healthy controls (mean age=64.7±3.34, male=63%) were recruited. The median and interquartile range of the markers in healthy controls and

CRC patients (at diagnosis and 6 months before) and TNM stage are shown in Table 1. Statistically significant differences ($p < 0.05$) were found with all the analyzed markers in cases and controls, also between cases at the time of cancer diagnosis and 6 months before, and finally between TNM stages.

Regarding the diagnosis utility; ROC curve analysis provided the following cutoff points (and AUC): NLR 2.28(AUC: 0.732), PLR 110.42(0.742), SII 616.46(0.744) and NP/LHb 43.9(0.785). All biomarkers obtain intermediate Se and NPV around 60-65% but high Sp and PPV; the best results were obtained with NP/LHb (Sp: 90.8 PPV: 86.8).

	NLR	PLR	SII	NP/LHb
Healthy controls	1.61 (1.23-2.18)	90.86 (75.31-110.4)	342.25 (238.96-493.88)	23.29 (15.76-33.07)
CRC: Analysis prior to diagnosis	1.90 (1.39-2.69)	110.86 (84.90-153.88)	441.04 (298.15-633.56)	33.03 (23.04-49.24)
CRC: Analysis at the time of diagnosis	2.57 (1.69-4.24)	133.76 (96.32-185.35)	618.75 (384.63-1086.08)	49.31 (27.97-96.83)
p	0.00	0.00	0.00	0.00
TNM I	1.8 (1.3-2.3)	110 (86-139)	414 (339-616)	30,69 (25.62-51.55)
TNM II	3 (1.8-5.6)	122 (89-189)	677 (317-1375)	55.95 (27.51-117.67)
TNM III	2.9 (1.9-4.4)	144 (104-184)	640 (412-1087)	50.15 (28.83-85.13)
TNM IV	2.7 (1.9-4.6)	158 (99-222)	941 (462-1360)	68.05 (37.21-117.70)
p	0.00	0.00	0.00	0.01

[Table 1. Blood Inflammatory biomarker indexes (median and interquartile ranges)]

Conclusion: When compared to healthy controls, inflammatory blood analytical biomarkers increase progressively during the development of CRC, showing higher values in patients with CRC at the moment of the diagnosis. The same trend was observed when comparing the different TNM stages. These non-invasive markers could be useful for the CRC diagnosis and prognosis. Because of its high Sp and PPV, the NP/LHb index could be a useful tool to combined with FIT, to prioritize colonoscopies in a CRC screening program.

Disclosure: Nothing to disclose

P0642

CLINICAL EFFICACY OF FECAL MICROBIAL TRANSPLANTATION TREATMENT IN ADULTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

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Introduction: Atopic dermatitis (AD) is a remitting relapsing chronic eczematous pruritic skin disease affecting over 20% of children and up to 10% of adults. Recent evidence suggests that the gut microbiota may have a role in AD by regulating the immune system. Atopic dermatitis (AD) is a remitting relapsing chronic eczematous pruritic skin disease affecting

over 20% of children and up to 10% of adults. Recent evidence suggests that the gut microbiota may have a role in AD by regulating the immune system.

Aims & Methods: We aimed to assess the efficacy and safety of fecal microbiota transplantation (FMT) for AD.

We performed the first-in-human prospective, single-blinded, placebo-controlled cross-over pilot study among ten adults who had moderate-to-severe AD, insufficiently responsive to topical and systemic treatment. All patients received 2 placebo FMTs followed by 4 FMTs from healthy donors each 2 weeks apart. During the study period patients were allowed to continue with their medical topical treatment, but no new therapy was commenced. The severity of AD was evaluated during the study period by the SCORing Atopic Dermatitis (SCORAD) score.

Results: Nine patients completed the study protocol. There was no significant change in the SCORAD score following placebo transplants ($2.5\% \pm 22.1\%$, $P=0.86$) but there was a significant reduction following four doses of FMT ($59.2\% \pm 34.9\%$, $P=0.01$). Metagenomic analysis of the fecal microbiota showed transmission of bacterial strains from donors to patients. No adverse events were recorded during the study and follow-up period.

Conclusion: FMT is safe and effective as a therapeutic intervention for moderate-to-severe AD patients. The therapeutic improvement may be associated with microbial strain transmission from donors to patients. Double-blind placebo-controlled studies are required to verify the importance of the gut microbiota in the pathogenesis of AD.

Disclosure: Nothing to disclose

P0643 WITHDRAWN

P0644

EFFECTIVE GROWTH INHIBITION OF CLOSTRIDIUM DIFFICILE BY INTESTINAL ISOLATES (LIVE FORM BACTERIA AND CELL-FREE SUPERNATANT) FROM HUMAN FECES

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Introduction: Clostridium difficile infection (CDI) has increased over the past decades. Fecal microbiota transplantation (FMT) is recognized as an alternative to antibiotics for the treatment of recurrent Clostridium difficile infection. Many researchers suggested that intestinal bacteria play an important role for CDI, but still not clear which bacteria is key microbiota or how they can alleviate infection disease. In this study, we investigated the antimicrobial ability of fecal isolates against the *C. difficile*.

Aims & Methods: Bacterial culture and cell-free supernatant of 11 strains isolated from human feces, namely, *Lactobacillus rhamnosus*, *L. sakei*, *L. crispatus*, *L. paragaseri*, *L. johnsonii*, *Bifidobacterium breve*, *B. adolescentis*, *B. bifidum*, *B. animalis*, and *B. pseudocatenulatum*, and *Ruminococcus*

gnavus were evaluated for *C. difficile* suppression. The pellet and cell-free supernatant of fecal isolates was collected by centrifugation at 4000 rpm at 4°C for 30 min. The pellets were washed three times with PBS, then, resolved and inoculated to BHI medium with *C. difficile*. Cell-free supernatants were prepared to concentrating with 100 KDa filter (Amicon® Ultra-15 centrifugal filter unit, Millipore) and *C. difficile* were inoculated. Cultures incubated for 24 hours under anaerobic conditions. Antimicrobial ability of test strain against *C. difficile* was determined to evaluate *C. difficile* growth.

Results: After co-culture, all the test strains grew well in co-culture and were observed 10^8 CFU/ml of bacterial density. *B. animalis ssp lactis*, *L. johnsonii* and *B. breve* were able to inhibit growth of *C. difficile* in the pellet and cell-free supernatant. Especially, *B. breve* significantly had suppressed *C. difficile* growth. *B. pseudocatenulatum* also highly suppressed to *C. difficile* growth in co-culture; however, there was no inhibition in the supernatant.

On the other hands, *B. adolescentis*, *L. rhamnosus*, *L. sakei* and *L. paragaseri* inhibited *C. difficile* growth in supernatant. *B. bifidum* and *Ruminococcus gnavus* was not observed in *C. difficile* inhibition at all.

Conclusion: In this study, we demonstrated that the fecal bacteria isolates such as *B. animalis ssp lactis*, *L. johnsonii*, *B. breve* had inhibitory effect on *C. difficile* growth. We also found out not only fecal bacteria cell, but also cell-free supernatants had been able to prevent *C. difficile* colonization. These results suggested the possibility of bacterial supernatant (*B. animalis ssp lactis*, *B. breve*, *L. johnsonii*) for the treatment of CDI instead of live bacteria. Also, These results provided a basal information of the bacterial consortium for CDI treatment.

Disclosure: Nothing to disclose

P0645

RIGHT-SIDED COLONIC BIOFILMS ARE ASSOCIATED WITH ADENOMA FORMATION IN PATIENTS WITH LYNCH SYNDROME

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Introduction: Colonic bacterial biofilms are an emerging manifestation in colorectal cancer (CRC); they exhibit carcinogenic properties and are frequently present on right-sided cancerous lesions. Whether bacterial biofilms propose a risk-factor for early carcinogenesis in humans is yet unresolved.

Aims & Methods: We studied bacterial biofilms in tandem with adenoma formation in patients with Lynch syndrome (LS). LS patients carry a pathogenic germline variant in one of the DNA mismatch repair (MMR) genes, resulting in a variable predisposition to develop colonic cancerous lesions. A total of 100 LS patients were included in our study, consisting of 23 *MLH1*, 24 *MSH2*, 36 *MSH6*, and 17 *PMS2* MMR variants. During regular screening colonoscopies, normal appearing forceps biopsies were taken from colon ascendens (right colon) and descendens (left colon). Biopsies were screened for bacterial biofilms using fluorescent *in situ* hybridization by targeting bacterial 16s rRNA. The frequency of colorectal adenomas (tubular adenomas and (tubulo)villous adenomas) before and during colonoscopy was registered.

Results: Overall, 60% of patients presented with a biofilm, of which most were right-sided (right-sided: 25%, both sides: 21%, left-sided: 14%). Interestingly, adenomas were more frequently present in patients with a right-sided biofilm (right-sided: 64%, both sides: 58%) than in patients with a

left-sided biofilm (29%) or no biofilm (38%). The occurrence of bacterial biofilms was not correlated with age, BMI or MMR-variant. Statistical analysis revealed that right-sided bacterial biofilms correlated with right-sided adenomas (pearson: 0.272, $p=0.007$) and left-sided adenomas (pearson: 0.227, $p=0.026$), while left-sided biofilms were not correlated with left- or right-sided adenomas (pearson: 0.037, $p=0.718$ and -0.127 , $p=0.213$). To model the probability of right-sided adenoma formation, we performed a binary logistic regression analysis and found that age (odds ratio: 1.065 (CI: 1.024; 1.108, $p=0.002$)) and right-sided biofilms (odds ratio: 3.020 (CI: 1.151; 7.926, $p=0.025$)) significantly contributed.

Conclusion: Our data suggest that right-sided bacterial biofilms are a hallmark for high-risk LS patients and may play a role in early carcinogenesis.

Disclosure: Nothing to disclose

P0646

MAPPING THE COLORECTAL TUMOUR MICROBIOTA

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Introduction: The gut microbiome in patients with colorectal cancer (CRC) is different from that of controls, supporting the hypothesis that altered microbial functions may play a role in CRC initiation or progression. Most previous studies have profiled the CRC tumour microbiome using a single biopsy. However, since the morphology and cellular subtype vary significantly within an individual tumour, the possibility of a sampling error arises for the microbiome within an individual tumour.

Aims & Methods: To investigate inter-tumoural microbial heterogeneity in CRC.

Seven biopsies were taken from representative areas on and off the tumour in five patients with CRC. Genomic DNA were extracted and underwent 16s rRNA gene PCR and sequencing. Raw data was imported into R v3.5.3 for processing and analysis.

Results: The microbiome composition was highly similar among samples within a particular individual. The genus level composition differed significantly between patients but was remarkably similar within a single subject both on and off the tumour site. This was reflected in beta diversity distance metrics wherein samples clustered by individual rather than biopsy site as represented in Principal Co-ordinate Analysis (PCoA) plots. This beta diversity clustering was supported by hierarchical clustering in which the topology of the dendrogram was clearly dictated by the subject identity rather than biopsy site. Within subjects, there was no reproducible pattern of microbiota relatedness by anatomical origin that was replicated across subjects. Furthermore, differential taxon abundance was not detected with respect to anatomical site when we applied paired sample Wilcoxon test with Benjamini-Hochberg adjustment for multiple comparisons. The difference in alpha-diversity of the biopsy microbiota datasets as measured by 5 different indices was significantly greater between any two individuals than it was within individuals.

Conclusion: This is the first study, to our knowledge, that shows that the microbiome of an individual tumour is spatially homogeneous. This finding strengthens the assumption of previous studies that a single biopsy

was representative of the entire tumour, and that microbiota changes are not limited to a specific area of the neoplasm.

Disclosure: Nothing to disclose

P0647

THE EFFECT OF SACCHAROMYCES BOULARDII CNCM I-745 ON ANTIBIOTIC-RELATED GUT MICROBIOTA DYSBIOSIS DEVELOPMENT: AN EXPERIMENTAL STUDY

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Introduction: Nowadays antibiotic treatment is widely prescribed worldwide, which leads to the increasing prevalence of antibacterial drug-related pathologies. It is postulated that antibacterial therapy is one of the most common reasons for gut microbiota dysbiosis development. Management of the latter aims to reduce the excessive number of microorganisms in the upper part of the gastrointestinal tract and recover the microbiota of bowel. Despite the fact that there are a number of dysbiosis treatment approaches, the effective strategy to recover gut microbiota is still debatable.

Aims & Methods: The purpose of this study is to investigate the preventive effect of *Saccharomyces boulardii* CNCM I-745 on gut microbiota dysbiosis development among patients receiving antibacterial treatment.

The current study utilizes an experimental design with a comparison group.

All the patients who applied to the department of Internal diseases of Qanaqer-Zeytun MC from January 2018 until December 2019 and received specific antibacterial therapy were enrolled. The cohort was divided into four subgroups and each of them received one antibacterial agent (i.e. aminopenicillins, macrolides, cephalosporins, and fluoroquinolones). Beforehand, all the patients underwent a stool culture test and those who had abnormal bacterial growth in feces were excluded from the study. The subjects were assigned identification numbers in accordance with their admission order. All the patients exposed to the antibiotic therapy with odd ID numbers were assigned to the treatment group and those with even ones were assigned to the comparison group. Those assigned to the treatment group received *S. boulardii* CNCM I-745 treatment simultaneously with antibacterial therapy and those in the comparison group did not receive any additional treatment.

On the twelfth day of the antibacterial therapy, all the subjects passed a stool culture test to assess bacterial growth in feces and development of gut microbiota dysbiosis. Data were analyzed through SPSS statistical software and the Fisher-Freeman-Halton test was performed to assess the preventive effect of *S. boulardii* on antibiotic-related gut microbiota dysbiosis.

Results: In total, data of 80 subjects were analyzed. The age range was 16-59 years, male/female ratio was 0.9. In the current cohort, 50% received *S. boulardii* treatment and the other 50% did not receive any supplementary treatment. Descriptive statistics of the subgroups are presented in the table. In the aminopenicillin group, *S. boulardii* treatment was significantly associated with the prevention of gut microbiota dysbiosis ($P = 0.029$). In the macrolide group, there were no cases of gut microbiota dysbiosis, which might be suggestive that the current agent does not lead to the microbiota disruption. In the cephalosporine and fluoroquinolone groups, association between treatment and outcome was not significant. In the main group of 80 patients, *S. boulardii* treatment reduces the risk of gut microbiota dysbiosis development by 74% ($RR=0.26$; 95% $CI=0.078-0.86$).

Gut microbiota dysbiosis patients	Aminopenicillin		Macrolide		Cephalosporin		Fluoroquinolone	
	N	Total	N	Total	N	Total	N	Total
S. boulardii treated	0	12	0	12	1	8	2	9
S. boulardii untreated	4	10	0	12	4	10	3	7

[Descriptive characteristics of antibiotic subgroups]

Conclusion: The study has shown that the application of *S. boulardii* effectively prevents antibiotic-related gut microbiota dysbiosis development and might be recommended in antibacterial treatment.

Disclosure: Nothing to disclose

P0648

EFFICACY AND SAFETY OF FECAL MICROBIOTA TRANSPLANTATION ON CLEARANCE OF MULTI-DRUG RESISTANCE ORGANISM IN MULTI-COMORBID PATIENTS: A PROSPECTIVE NON-RANDOMIZED COMPARISON TRIAL

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Introduction: Multi-drug Resistance Organism (MRDO) carriage could be the fatal pathogen as hospital infection. Fecal microbiota transplantation (FMT) has been reported to be a possible option for decolonization.

Aims & Methods: This study aimed to whether FMT is effective and safe to eradicate intestinal colonization of MRDO. A total of 21 patients with MRDO colonization such as carbapenem-resistant *Enterobacteriaceae* (CRE) or vancomycin-Resistant *Enterococci* (VRE) were included in FMT group from July 2019 to April 2020. 14 patients were included as control groups. All of the enrolled patients were confirmed two consecutive colonization before inclusion followed for more than 1 month. The primary end point was negative conversion in stool culture within 1 months. The secondary end point was negative conversion in stool culture after 3 months and possible adverse events during follow-up within 3 months.

Results: FMT group included 13 CRE patients (11/21, 52.3%), 5 VRE patients (5/21, 23.8%) and 3 patients CRE and VRE (3/21, 14.2%). Among them, 2 patients (1 CRE /VRE and 1 VRE) died by the causes unrelated to FMT within 1 month and 1 patient with CRE and VRE died due to underlying disease and 1 patient was follow-up loss. Control group included 7 CRE patients (7/17, 41.1%) and 10 VRE patients (10/17, 58.8%). During follow-up period, 1 CRE patients died within 1 month and 4 VRE patient died after 1 month due to their underlying disease. 2 patients (1 CRE and 1 VRE) were not follow-up after 1 months.

Overall negative conversion within 1 month (40% (8/20) vs 0% (0/14)) and 3 months (28.6% (10/14) vs 11.1% (1/9)) was significantly different between FMT and control groups ($P=0.02$ and $P=0.09$, respectively) Among patients with CRE, 5 patients (5/7, 41.7%) in FMT group and no patients in control group was decolonized within 1 months ($P=0.06$). However, 8 patients (8/9, 88.9%) in FMT group achieved negative conversion within 3 months, compared with 1 patient (1/4, 25%) in control group ($P=0.02$). Among patients with VRE, 3 patients (3/5, 37.5%) in FMT group and no patients in control group was decolonized within 1 months ($P=0.07$).

During post-FMT follow-up period, 5 patients (23.8%) had a non-infected fever and 4 patients (19%) had diarrhea within 1 weeks. 4 patients had infection (1 pneumonia, 1 cholecystitis, 2 urinary tract infection), and were treated by antibiotics or operation within 1 months. Some patient had gout attack.

Conclusion: FMT could be effective for MRDO decolonization in intestinal tract. It is not sure if these adverse effects shown above are related to FMT, but multi-morbid patients need close monitoring for a certain period after FMT. These data should be confirmed by larger and randomized controlled trials.

Disclosure: Nothing to disclose

P0649

DEVELOPMENT OF A PANEL OF MICROBIAL MARKERS TO DISTINGUISH TEMPORARY FROM PATHOLOGICAL DYSDIOSIS

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Introduction: Dysbiosis is a widely used but unspecific term. It has been defined as any change in the composition of resident microbial commensal communities relative to the ones found in healthy individuals. But it is still unclear which are the appropriate communities to define it and the tolerance values to measure it. Different studies have described dysbiosis in various diseases such as Inflammatory Bowel Disease (IBD), rheumatoid arthritis and autism among others. It was also reported that microbiota switches from eubiosis to dysbiosis by environmental factors such as antibiotic treatment, low fiber intake diet, stressed lifestyle or infections. Therefore, different severity grades can be associated with the term dysbiosis from which pathological and temporary dysbiosis can be differentiated.

Aims & Methods: This work aimed at defining a more specifically the term intestinal dysbiosis and to differentiate both temporary and pathological dysbiosis. Fifteen key microbial markers belonging to the principal families, classes and orders found in the human intestinal microbiota were accurately selected based on its functionality: *F.prausnitzii* (Fpra), *E.coli* (Eco), Firmicutes (Fir), Bacteroidetes (Bac), *A.muciniphila* (Akk), *Ruminococcus* sp. (Rum), *Roseburia* sp. (Ros), Gamma-proteobacteria (Gam), *Clostridia* cluster I (Clo), *Clostridia* cluster XIV (XIV), *Enterococcus* sp., *Lactobacillus* (Lac), *C.albicans* (Can), *M.smithii* (Msm) and the total bacterial load (Eub).

The dysbiosis was defined in a cohort of healthy subjects (24 stool samples) and then validated with 9 patients diagnosed with intestinal disease (6 IBD and 3 Irritable Bowel Syndrome stool samples). The samples were collected by the Hospital Universitari Dr. Josep Trueta. Total DNA was extracted and the abundance of microbial markers was analysed by qPCR. All the abundances were normalized using the average of 16S rRNA gene copies found in the target species of the microbial markers and the amount of sample.

Besides establishing the most common range in which each microbial marker was found, an index to define the pathological dysbiosis was calculated. The so-called Fpra-Eco index (FEI) consisted of subtracting the final logarithmic abundance of Eco from that of Fpra. Higher values indicate healthy situations, whereas lower values tells about the presence of pathological dysbiosis.

Results: Almost all the healthy population tested presented one or two slightly altered bacterial markers. These alterations are found to be close to the established range but still outside and defined temporary dysbiosis. The most common microbial markers in this temporary dysbiosis were Fpr, Firm, Akk, Ros, Gam and Msm. Fpr, Akk and Ros are indicative of the mucous layer state, Firm is indicative of the lifestyle and fiber intake, Gam is indicative of the pro-inflammatory state of the gut and Msm is indicative of an altered intestinal habit and gas production.

All the analyzed patients (IBD and IBS) presented alterations mainly of the bacteria inhabiting the mucosa indicating gradient disruption of the mucous layer. An alteration of the abundance of proteolytic bacteria can also mean a reservoir of some potentially pathological bacteria and an alteration of the opportunistic species related to the disrupted mucous layer.

Conclusion: This study establishes an appropriate abundance range of key microbial markers in the gut, leading to a specific definition of dysbiosis, which allows to differentiate the pathological from the temporary dysbiosis, by using the FEI. These results need further validation in a larger patient cohort.

Disclosure: Nothing to disclose

P0650

DIARRHEA DURING *H. PYLORI* ERADICATION THERAPY AND HUMAN GUT MICROBIOTA COMPOSITION AND FUNCTIONAL POTENTIAL ALTERATIONS

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Introduction: It is well known that antibiotics could cause adverse events such as diarrhea, which is one of the most frequent.

Aims & Methods: The aim of the study was to identify differences of the gut microbiota composition and functional potential during *H. pylori* eradication therapy in patients with diarrhea vs without adverse events.

Stool samples were collected from 102 patients before and immediately after *H. pylori* eradication therapy (amoxicillin 1000 mg, clarithromycin 500 mg, proton pump inhibitor, bismuthate tripotassium dicitrate 240 mg bid for 14 days). DNA was extracted from stool samples and sequenced on SOLiD 5500xl-W. Relative abundance of metabolic pathways (MP) which were classified according to MetaCyc database and abundance of bacterial genera were evaluated in the gut microbiota before and immediately after the eradication therapy; $p < 0.05$ was considered statistically significant.

Results: A total of 7 (6.9%) patients had diarrhea during eradication therapy. The relative abundance of *Enterococcus* and *Cellulophaga* genera was significantly higher before eradication therapy in case of patients with diarrhea during therapy compared to patients without adverse events: $(0.22 \pm 0.36)\%$ vs $(0.07 \pm 0.23)\%$, $p = 0.04$ and $(0.003 \pm 0.007)\%$ vs 0 , $p = 0.004$, respectively. The abundance of 22 MP, including 14 biosynthesis MP: sugar nucleotide (PWY-6138: CMP-N-acetylneuraminate biosynthesis I, PWY-7316: dTDP-N-acetylvirosamine biosynthesis), ubiquinol (PWY30-19: ubiquinol-6 biosynthesis from 4-hydroxybenzoate), NAD (NAD-BIOSYNTHESIS-II: NAD salvage pathway II, PWY-5381: pyridine nucleotide cycling), fatty acids (8 MP) and cell structure (1 MP) were also more represented in patients with diarrhea ($p < 0.05$).

Five Degradation/Utilization/Assimilation MP: amino acids (LYSINE-DEG1-PWY: L-lysine degradation XI), aromatic compounds (PWY0-321: phenylacetate degradation I), phosphorus compounds (PWY-7399: methylphos-

phonate degradation II), fatty acids (PWY-5136: fatty acid β -oxidation II), purine (PWY-6353: purine nucleotides degradation I); two Generation of Precursor Metabolite and Energy MP (PWY-6859: all-trans-farnesol biosynthesis, P163-PWY: L-lysine fermentation to acetate and butanoate) and nucleic acid processing (PWY-7283: wybutosine biosynthesis) MP were more represented in patients with diarrhea than in patients without this adverse event ($p < 0.05$).

Immediately after the eradication therapy abundance of *Collinsella* genus was significantly higher in patients without adverse events than in patients who had diarrhea during the treatment: $(0.11 \pm 0.45)\%$ vs 0 , $p = 0.044$. At the same time abundance of five MP: biosynthesis of carbohydrate (GLYCOGENSYNTH-PWY: glycogen biosynthesis I, CALVIN-PWY: Calvin-Benson-Bassham cycle), amino acids (BRANCHED-CHAIN-AA-SYN-PWY: superpathway of branched amino acid biosynthesis, SER-GLYSYN-PWY: superpathway of L-serine and glycine biosynthesis I) and pentose phosphate MP (NONOXIPENT-PWY: pentose phosphate pathway) was higher in patients without diarrhea.

However, four MP: biotin biosynthesis (PWY-5005: biotin biosynthesis II), L-arginine degradation (ARGORNPROST-PWY: arginine, ornithine and proline interconversion), nicotine degradation (PWY66-201: nicotine degradation IV), nucleic acid processing MP (PWY-7379: mRNA capping II) were predominant after the therapy in patients with diarrhea.

Conclusion: So significant differences were found in the gut microbiota composition and functional potential before and immediately after *H. pylori* eradication depending on the presence of diarrhea during the therapy, which could be linked with diarrhea development during the therapy.

Disclosure: Nothing to disclose

P0651

A DISTINCT INTESTINAL MICROENVIRONMENTAL PROFILE IS LINKED TO BOWEL HABITS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Patients with irritable bowel syndrome (IBS) are suggested to have an altered intestinal microenvironment compared to healthy subjects. Previous studies have explored either microbiota composition or metabolic parameters, but none has yet studied these variables in combination, in IBS patients of all subtypes.

We therefore aimed to determine the overall intestinal microenvironment profile, including fecal microbiota and metabolites, in IBS patients (all subtypes) and healthy subjects, and the potential link to symptoms related to IBS.

Aims & Methods: Fecal samples were collected from IBS patients fulfilling the ROME III criteria (all subtypes) and healthy subjects. Fecal microbiota was evaluated by GA-map™ Dysbiosis Test, while tandem mass spectrometer (GC-MS/MS) was used for metabolomic profiling. Symptom sever-

ity as well as anxiety and depression in IBS patients was assessed by IBS Severity Scoring System (IBS-SSS) and Hospital Anxiety and Depression Scale (HADS), respectively. Patients were characterized according to Rome III IBS subtypes based on predominant bowel habits using the Bristol Stool Form (BSF) scale (IBS with constipation (IBS-C) or diarrhea (IBS-D), Mixed IBS (IBS-M) or Unsubtyped IBS (IBS-U). Multivariate analyses were applied to the data set comprising fecal microbiota and metabolites to identify patterns and relationships between the variables. Ingenuity Pathway Analysis Core Analysis (IPA, version 2.3) (Qiagen) was carried out to identify biological functions associated to metabolomic differences between IBS patients and healthy subjects.

Results: A principal component analysis of the intestinal microenvironmental profile, comprising fecal microbiota (n = 54) and metabolites (n = 155), showed that IBS patients (n=40) and healthy subjects (n=18) tended to cluster separately. As shown in table 1, a large number of metabolites along with a few bacterial taxa were found in higher levels in IBS patients, whereas only a few variables were lower in IBS patients as compared to healthy subjects.

Thus, the distinct intestinal microenvironmental profile of IBS patients was mostly driven by metabolites. Additionally, the intestinal microenvironmental profile differed between IBS-C (n=15) and IBS-D (n=11), where IBS-D patients were mainly defined by higher levels of several metabolites and few bacterial taxa as compared to IBS-C patients (Table 1). However, no clustering based on fecal bacteria and metabolites was seen when patients were subgrouped according to symptom severity or anxiety and depression.

Further, IPA Core Analysis predicted amino acid metabolism and several cellular and molecular functions to be altered in IBS patients based on differences in the metabolite profile between patients with IBS and healthy subjects.

Intestinal microenvironmental profile	↑IBS*	↓IBS*	↑IBS-D ^o	↓IBS-D ^o
Bacterial taxa (no.)	3	5	2	4
Metabolites (no.)	67	2	27	5

The number (no.) of bacterial taxa (n=54) and metabolites (n=155) being different in IBS patients (n=40) as compared to healthy subjects (n=18)*, as well as variables being different in IBS patients with diarrhea (IBS-D, n=11) compared to IBS patients with constipation (IBS-C, n=15)^o. Upward pointing arrow represents upregulation and downwards arrow represents downregulation.

[The intestinal microenvironmental profile is distinct in patients with irritable bowel syndrome and is linked to bowel habits]

Conclusion: The intestinal microenvironment, including microbiota and metabolites, differentiates IBS patients from healthy subjects, as well as discriminates IBS subgroups based on the predominant bowel habit. Moreover, IPA Core Analysis predicted amino acid metabolism and certain cellular and molecular functions to be of importance in the pathophysiology of IBS.

Disclosure: Nothing to disclose

P0652

BILE ACIDS METABOLIZING BACTERIA ABUNDANCE IN THE GUT MICROBIOTA ON THE BACKGROUND OF *H. PYLORI* ERADICATION THERAPY

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Introduction: Bile acids play an important fundamental role in human body, including involvement in the intestinal absorption of lipids and lipophilic vitamins. The gut microbiota can modify bile acids content through biotransformation reactions. Several diseases associated with gut microbiota changes as well as temporary use of antibiotics can lead to the disorders of bile acids ratio and composition.

Aims & Methods: The aim of the study was to assess the influence of *H.pylori* eradication therapy on the abundance of bile acids metabolizing bacteria in the gut microbiota.

Stool samples from 102 *H.pylori*-positive patients before and immediately after eradication therapy (amoxicillin 1000 mg, clarithromycin 500 mg, bismuthate tripotassium dicitrate 240 mg, proton pump inhibitor bid for 14 days), and 29 stool samples one month after therapy from the same patients were collected. Stool biosamples were analyzed using shotgun metagenomic sequencing (SOLiD 5500 Wildfire platform). Relative abundance of bacterial genera involved in the bile acids metabolism were evaluated in the gut microbiota before, immediately after and one month after the *H.pylori* eradication therapy; p< 0.05 was considered statistically significant.

Results: Nine bacterial genera involved in the bile acids metabolism were identified in the gut microbiota: *Alistipes*, *Bacteroides*, *Bifidobacterium*, *Clostridium*, *Escherichia*, *Eubacterium*, *Lactobacillus*, *Peptostreptococcus*, *Ruminococcus*. The relative abundance of *Bifidobacterium*, *Eubacterium*, *Ruminococcus* significantly decreased immediately after therapy comparing with baseline – 0.32±1.24% vs 2.56±5.35%, p=3.60E-16; 9.99±13.65% vs 14.30±11.50%, p=5.90E-05; 3.88±5.50% vs 5.96±6.17%, p=0.0008, respectively. However relative abundance of *Bacteroides* and *Escherichia* increased immediately after eradication therapy – 22.10±20.38% vs 13.96±16.55%, p=0.015 and 5.31±12.75% vs 1.68±6.06%, p=0.0033, respectively. Tendency to return to the initial level was observed in a month after the eradication therapy for most of bacterial genera except *Bifidobacterium* which abundance remained below the baseline level – 1.33±3.09% vs 2.56±5.25%, p=0.0041. No changes were found in relative abundance of *Alistipes*, *Clostridium*, *Lactobacillus*, *Peptostreptococcus* on the background of eradication therapy.

Conclusion: So *H.pylori* eradication therapy leads to significant changes in abundance of bile acids metabolizing bacteria in the gut microbiota. Further studies need to be performed to evaluate clinical significance of these changes.

Disclosure: Nothing to disclose

P0653

SHIFTS IN RESISTANCE OF *LACTOBACILLUS* IN HUMAN GUT MICROBIOTA AFTER *HELICOBACTER PYLORI* ERADICATION THERAPY

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Introduction: *Lactobacillus* are typical representatives of human intestinal, oral and urogenital resident microbiota. One of the most important functions of *Lactobacillus* is a participation in the processes of systemic and local immune response of the human body.

In this regard, the use of *Lactobacillus* for therapeutic purposes as probiotics has become widespread. Due to the growing antibiotic resistance, there is considerable interest to investigate the formation of resistome in commensal bacteria.

Aims & Methods: The aim of this study was to determine the possibility of occurrence of *Lactobacillus* resistant forms in the intestinal microbiome after *H. pylori* eradication therapy.

For this purpose, eighteen stool samples from *H. pylori*-positive patients before (n=9) and after (n=9) eradication therapy (standard Maastricht V protocol) were collected. Metagenomic sequencing was performed on Nextseq 500 platform (Illumina, USA), according to the manufacturer's recommendations, followed by the use of the MetaPhlAn2 package for microbial community profiling.

Lactobacillus strains were isolated from the stool samples of patients and cultured at 37°C on Man-Rogosa-Sharpe medium (MRS). Screening for antibiotic resistance was performed on the medium with clarithromycin (1.4 µg / ml) and amoxicillin (3.6 µg / ml). Isolated microorganisms were identified using a MALDI Biotyper system (Bruker Daltonik GmbH, Germany).

Results: Metagenomic shotgun sequencing revealed a decreased proportion of *Lactobacillus* in the intestinal microbiota community after eradication therapy in 44.4% (n=4) of patients.

However, in 44.4% (n=4) of patients after therapy there was an increase in the abundance of *Lactobacillus*, to varying degrees. In 11.2% (n=1) of patients, *Lactobacillus* were absent, both before and after eradication therapy. In the intestinal microbiota of patients before eradication, the most common species were *L. fermentum* (33.3%), *L. gasseri* (33.3%), *L. salivarius* (33.3%), *L. vaginalis* (33.3 %), and *L. ruminis* (22.2%); after eradication, the most common were *L. fermentum* (55.6%), *L. casei paracasei* (33.3%), *L. curvatus* (22.2%), *L. oris* (22.2%), and *L. plantarum* (22.2%).

However, according to metagenomic data, *Lactobacillus* constitute a small fraction of the intestinal microbiota (< 1%), which does not allow the identification of all intestinal *Lactobacillus* by this method.

For group of patients with decreased proportion of *Lactobacillus* after therapy, in stool samples before the eradication *L. gasseri*, *L. johnsonii*, *L. plantarum*, *L. salivarius* and *L. rhamnosus* were isolated by cultivation method. After the eradication, *Lactobacillus* (*L. mucosae*) were found only in one out of 4 patients.

From 2 out of 4 patients with an increased proportion of *Lactobacillus*, *L. fermentum* and *L. rhamnosus* were isolated from stools samples before the eradication therapy. After the therapy only *L. plantarum* was found.

For one patient with no detected *Lactobacillus* in gut microbiota before and after antibiotic therapy, according to the metagenomic data, *Lactobacillus* strains were not detected by culture method as well.

None of the isolated *Lactobacillus* strains possessed phenotypic resistance to clarithromycin and amoxicillin.

Conclusion: *H. pylori* eradication therapy leads to shifts in the composition of the *Lactobacillus* community due to the complete replacement of some species by others. These changes after two-week antibiotic therapy are not associated with the resistance acquirement in commensal bacteria and may have a transitory nature.

Disclosure: This work was funded by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities (project №0671-2020-0058)

P0654 WITHDRAWN

P0655

ENTAMOEBA HISTOLYTICA COLITIS - 10-YEAR CASE SERIES FROM A TEACHING HOSPITAL IN A NON-ENDEMIC REGION

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Introduction: Invasive *Entamoeba histolytica* (EH) is a recognised cause of infectious colitis and abscess formation. It is transmitted faeco-orally and is responsible for significant mortality and morbidity predominantly in endemic regions, but its occurrence in non-endemic regions is uncommon and poorly characterised. We report a 10-year retrospective case series of intestinal EH at a regional hospital in London UK and describe its associated risk factors.

Aims & Methods: A search of microbiology, histopathology and endoscopy databases was performed to identify all patients (pts) with positive EH serology (IFAT, CAP), stool EH DNA PCR (introduced 2018), and histology taken at colonoscopy consistent with EH colitis, between 01/01/2009 and 31/12/2019. We examined patient demographics, presenting symptoms, travel history/ethnicity, past medical history, treatment and colonoscopic findings.

Results: Over this 10-year period, 16pts had EH colitis (of which 3 also had liver abscess), 15pts had EH liver abscess, and 1pt had a cerebral abscess. We characterised pts with EH colitis. Age range was 26-77years (median 54years) and 11/16 male. 7/16 had travelled to endemic regions in the past year. 8/16 were from an endemic region but had not travelled in the past year. The most common symptoms were diarrhoea (7/16) and rectal bleeding (5/16). 2pts were asymptomatic and diagnosed on screening colonoscopy. 1pt had caecal ulceration with EH and adenocarcinoma. 2pts were initially misdiagnosed and treated for inflammatory bowel disease (IBD), and 1 for angiodysplasia. EH serology was positive in 9/16 and not checked for 7/16. Colonic histology found EH cysts or trophozoites in 12/16. EH stool DNA PCR was positive in both pts tested. Amoebic cysts were seen in 2/16, not seen in 6/16 and not checked for 8/16. Treatment varied and most commonly involved metronidazole (10/16). Cysticidal drugs were not given at diagnosis in at least 9pts (4 recurrence).

Conclusion: A careful travel history is important to exclude EH in non-endemic regions. Serology and colonic histology are accurate markers for EH colitis. Right-sided colonic inflammation was the most common endoscopic finding. EH stool DNA PCR where available is an accurate non-invasive test. Clinical features and colonoscopic features can mimic IBD and an index of suspicion is required to avoid misdiagnosis with serious

consequences. Treatment must include a cysticidal drug to avoid auto-reinfection which can be overlooked. Further national studies from non-endemic regions are required.

Disclosure: Nothing to disclose

	Colonic inflammation				
	Left sided only	Right sided only	Caecal only	Patchy colonic	Unknown
Colonoscopy	1	3	6	1	1
Fx Sigmoidoscopy	3	-	-	-	0

(*1pt had an ultrasound showing caecal inflammation with no endoscopy)

[Endoscopic Findings* (N=15)]

P0656

CLOSTRIDIODES DIFFICILE INFECTION IN THE BASQUE COUNTRY: CHARACTERISTICS, TREATMENT AND RECURRENCE

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Introduction: Clostridioides difficile infection (CDI) is one of the leading causes of healthcare-associated infections all over the world. The increasing incidence and recurrence rates of CDI over the last years, together with its associated morbidity and mortality, represent a great concern. In the last years the guidelines recommend against using metronidazole for the treatment of CDI.

Aims & Methods: The aim of this study is to evaluate the treatments used in our region and to know the recurrence rate of CDI.

We performed a multicenter, retrospective, observational study including all cases of CDI registered in 7 hospitals located in the region of Basque Country (Northern Spain), from January to December 2018 with a follow-up period of 8 weeks.

We analyzed epidemiological characteristics, risk factors, treatments and recurrences.

Results: We included 385 patients, 199 (51.7%) female and 186 male, mean age 67 years. Charlson index media 4.

64.4% (248/385), received previous antibiotic treatment. Other risk factors for CDI accounted were use of proton pump inhibitors 49.4% (190/385) and immunosuppression (onco-hematological disease, liver cirrhosis, transplantation, HIV, autoimmune disorders...) 25.7% (99/385).

The infection was healthcare-associated in 38.4% (148/385) and community acquired in 61.6% (237/385).

7 patients, (1.8%), needed colectomy. ICD directly associated mortality index was 4.1% (16/385) and elevated up to 15.3% (59/385) related to ICD in 90 days after infection.

First line treatment: 56.6 % (218/385) received metronidazole, 28.1% (108/385) vancomycin, 2.6% (10/385) fidaxomicin and 7.9% (49/385) others.

Overall recurrence rate 24.2% (93/385): 24.8% in metronidazole group (54/218), 25% (27/108) in vancomycin and 20% (2/10) in fidaxomicin.

Conclusion: CDI is a common cause of diarrhea in both inpatient and out-patient settings.

The age> 65 years, the chronic use of PPI, previous antibiotic use and immunosuppression are the most related risk factors for this infection.

The recurrence rates with the use of metronidazol and vancomycin in first episode in our region are similar.

Disclosure: Nothing to disclose

P0657

PREVENTION OF RECURRENT CLOSTRIDIODES DIFFICILE INFECTION AT TWO YEARS AFTER TREATMENT WITH INVESTIGATIONAL MICROBIOTA-BASED DRUG RBX2660: EFFICACY, DURABILITY, MICROBIOME CHANGES, AND PARTICIPANT DEMOGRAPHICS OF A PHASE 2 OPEN-LABEL CLINICAL TRIAL

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Introduction: Clostridioides difficile infection (CDI) is a global disease associated with mortality, morbidity, compromised quality of life, and substantial medical cost. Disruption of the intestinal microbiome contributes to recurrent CDI (rCDI), motivating development of microbiota therapies to prevent rCDI in individuals at high risk for recurrence.

We present the 24-month analysis of safety, efficacy, and microbiome restoration from a Phase 2 open-label trial of the investigational microbiota-based drug RBX2660 for prevention of rCDI. To address potential demographic differences on treatment outcome and durability, we also report a subpopulation analysis.

Aims & Methods: This multicenter, open-label Phase 2 trial included participants with multi-recurrent CDI who received ≤2 doses of RBX2660 delivered via enema 7 days apart. Efficacy was defined as absence of CDI recurrence through 8 weeks after the last dose. Durability was defined as continued CDI absence beyond 8 weeks.

Safety and durability assessments occurred at 3, 6, 12, and 24 months. A general linear model was performed to assess the influence of sex(female, male), age(≥65 years, < 65 years), and their interaction on clinical outcome.

Participant stool samples were collected prior to and for up to 24 months after treatment, and microbiome changes were assessed by shallow shotgun sequencing.

Results: As previously reported, the 8-week efficacy to prevent rCDI (79%;112/142) was higher than the CDI-free rate in the historical control group (31%, 23/75; $p < .0001$). Ninety-seven participants who achieved treatment success at 8 weeks were evaluable for long-term durability of whom 8 experienced a new CDI episode between 8 weeks and 24-months (92% overall durability).

Age and sex did not have a statistically significant impact on primary efficacy or durability. The safety profile of RBX2660 was acceptable up to 24 months and consistent with prior reports of microbiota-directed treatments; gastrointestinal disorders were the most common treatment-emergent adverse event organ class.

Microbiome analysis (503 samples from 110 primary treatment responders) showed that the relative abundance of Bacteroidia and Clostridia increased significantly within 7 days of treatment relative to baseline, concomitant with a decrease of Gammaproteobacteria and Bacilli, with maintenance of these changes throughout 24 months.

Conclusion: The microbiota-based drug RBX2660 demonstrated clinical durability in preventing rCDI at 24 months. This maintained efficacy was associated with sustained shifts in microbiome composition following treatment. Importantly, neither efficacy nor durability was dependent on age or sex.

Disclosure: This analysis was funded by Rebiotix Inc., Roseville, MN.

P0658 WITHDRAWN

P0659

PSEUDOMEMBRANOUS COLITIS: CLINICAL CHARACTERISTICS AND FACTORS ASSOCIATED TO SEVERE FORMS AND RECURRENCE OF THE DISEASE

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Introduction: Pseudomembranous colitis is the most common cause of diarrhea associated with the use of antibiotics worldwide. In the last few years, there have been reports of more severe forms of presentation of the disease and a greater recurrence of cases, associated with more virulent strains of *Clostridium difficile*.

Aims & Methods: All cases of pseudomembranous colitis that occurred in a central hospital in the last 5 years (primary or secondary diagnosis) were retrospectively studied in order to understand the clinical characteristics and factors associated with more severe or recurrent disease.

Results: A total of 108 patients with a diagnosis of pseudomembranous colitis were included, of which 5 (4.6%) had recurrent episodes and 8 (7.4%) had severe forms of presentation. The majority of patients (76%) were over 65 years old and 20.4% had a history of taking cephalosporins in the last 3 months; antibiotics of the penicillin class were used prior to diagnosis in 37% of cases and quinolones and meropenem in 12% each. The main reasons for taking antibiotics were respiratory infections (25%) and urinary tract infections (18.5%). The most used means of diagnosis were stool tests to detect toxins (38.9%), toxigenic cultures (25%) and colonoscopy (11.1%). The treatment of pseudomembranous colitis was done with metronidazole in 63.9% of the cases, vancomycin in 18.5% and their association in 12%.

Regarding factors associated with more severe episodes (fulminant toxic colitis and bowel perforation, sepsis) there was a higher percentage of patients who took metronidazole in combination with vancomycin to treat pseudomembranous colitis, compared to patients without severe forms of presentation ($\chi^2(8)=22.535$, $p=0.004$; effect size: $\phi=0.457$). None of the factors studied had a statistical impact on recurrent cases.

Conclusion: Pseudomembranous colitis is one of the main infections associated with health services, with alarming mortality and recurrence rates. This study aims to contribute to the adoption of more appropriate preventive and therapeutic strategies.

Disclosure: Nothing to disclose

P0660

POST-POLYPECTOMY BLEEDING OF COLORECTAL POLYP IN PATIENTS WITH CONTINUOUS WARFARIN AND SHORT-TERM INTERRUPTION OF DIRECT ORAL ANTICOAGULANTS

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Introduction: Post-polypectomy bleeding (PPB) is the most common complication after colorectal polypectomy. The use of anticoagulants is one of the important risk factors for PPB. This study aimed to evaluate PPB in patients with warfarin and direct oral anticoagulants (DOACs).

Aims & Methods: Between August 2017 and July 2019, a total of 12,601 polyps in 5,449 patients who underwent endoscopic snare resection of colorectal polyps were enrolled. Endoscopic snare resection was performed in patients with continuous warfarin (C-Warfarin) and with one-day of drug withdrawal of (O-) DOACs in accordance with the Japanese Gastroenterological Endoscopy Society (JGES) guideline.

Results: The PPB rate in the group with anticoagulants was statistically higher than that in the group without anticoagulants (8.5% [33/387] vs 1.2% [63/5,062]; $P < 0.001$). In multivariate logistic regression, male gender (odds ratio [OR]: 2.17; $P = 0.007$), warfarin (OR: 4.64; $P < 0.001$), DOACs (OR: 6.59; $P < 0.001$), and multi-polyp removal (OR: 1.77; $P = 0.007$) were the significant risk factors for PPB. PPB was observed in 9 and 21 patients in the C-Warfarin and O-DOAC groups; C-Warfarin (8.0% [9/113]), O-Dabigatran (6.1% [2/33]), O-Rivaroxaban (14.8% [9/61]), O-Apixaban (9.8% [9/92]), and O-Edoxaban (1.8% [1/56]). The PPB rate in the O-Rivaroxaban group was significantly higher than that in the O-Edoxaban group ($P < 0.05$).

Conclusion: Anticoagulant therapy was an independent risk factor for PPB. The rates of PPB in patients with C-Warfarin and O-DOACs were also higher than that in those without anticoagulants. Edoxaban may be safe for using short-term withdrawal in endoscopic snare resection of colorectal polyps.

Disclosure: Nothing to disclose

P0661

COLORECTAL POLYPECTOMY WITH CONTINUOUS WARFARIN COMPARED WITH HEPARIN BRIDGE THERAPY

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Introduction: Anticoagulant agents are one of the risk factors for delayed bleeding after endoscopic colorectal polypectomy. Heparin bridge therapy (HBT) as an alternative to warfarin is associated with high incidence rates of delayed bleeding. The newer guideline of Japanese Gastroenterological Endoscopy Society (JGES) recommends that a high risk of endoscopic procedures including colorectal polypectomy is allowed to perform with continuous warfarin when the international normalized ratio (INR) levels showed the therapeutic range (< 3.0).

Aims & Methods: This study aimed to evaluate delayed bleeding in patients with continuous warfarin compared with HBT.

Between January 2012 and July 2019, 206 polyps in 81 patients with continuous warfarin and 153 polyps in 60 patients with HBT who underwent endoscopic snare resection of colorectal polyps were enrolled.

Results: The rates of concomitant antiplatelet therapy is not significantly different between the continuous warfarin and HBT groups (38.2% [31/81] vs. 45.0% [27/60]; $P = 0.490$). The average numbers of removed polyps in the continuous warfarin and HBT groups were 3.3 and 3.6, respectively ($P = 0.983$). On the other hand, the average polyp size revealed a significant difference between the continuous warfarin and HBT groups (6.84 mm vs. 8.05 mm; $P = 0.001$). The polyps located in the right side of the colon in the continuous warfarin group was significantly higher than those in the HBT group (68.4% [141/206] vs. 46.4% [71/153]; $P < 0.001$). The delayed bleeding rate was not significantly different between the continuous warfarin and HBT groups (11.1% [9/81] vs 13.3% [8/60]; $P = 0.795$). However, the days of hospitalization in the HBT group was significantly longer than those in the continuous warfarin group (8.17 days vs. 3.69 days; $P < 0.001$). Neither refractory bleeding nor thromboembolic events was observed in every case.

Conclusion: Although statistically significant difference was not observed in the rate of delayed bleeding between the two groups, the days of hospitalization was significantly shorter in the warfarin group. Colorectal polypectomy with continuous warfarin may be safe and feasible.

Disclosure: Nothing to disclose

P0662 WITHDRAWN

P0663

MODIFIED PRE-ENDOSCOPIC ROCKALL SCORE IN PREDICTING THE OUTCOME OF PATIENTS WITH ACUTE LOWER GASTROINTESTINAL BLEEDING: A DIAGNOSTIC ACCURACY STUDY

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Introduction: Although the incidence of acute lower gastrointestinal bleeding (LGB) is increasing, the predictors of outcomes are not as well studied and defined as for acute upper gastrointestinal bleeding. At admission hemoglobin level as a predictor strong of severe bleeding. However the pre-endoscopic Rockall score does not include the hemoglobin value as a variable.

Aims & Methods: We hypothesised that a modified pre-endoscopy Rockall score (RockMOD) that include the levels haemoglobin might perform as well as other current scoring systems. The aim of this study was to compare the accuracy of RockMOD with four available risk scores (State, Oakland, Glasgow-Blatchford and Pre-endoscopic Rockall) for predicting severe LGIB, rebleeding, the need of transfusion and the need of treatment (endoscopic therapy, vascular embolization, surgery) in patients admitted for acute LGB.

Retrospective study from January 2013 to December 2017 in a university tertiary care hospital. Patients with acute LGB were identified using the International Classification of Diseases (9th Revision) and Clinical Modification codes for admission diagnosis. Scores were retrospectively calculated

according to the clinical reports data. Area under the receiver operating characteristic (AUROC) curve, sensitivity, specificity, positive and negative predictive values were calculated. Also the best cut-off for RockMOD was chosen from using the AUROC curve values. AUROCs were compared with the DeLong method by using STATA 14.1 software (StataCorp.2015).

Results: A total of 406 consecutive patients admitted with LGB were identified. Median age was 76.6 years (range 23-97), 277 (68.1%) of patients were older than 70 years, 219 (53.8%) were men. Six (1.5%) died, 36 (8.8%) rebleeding, 20 (4.95) needed readmission, 110 (27%) needed transfusion, 52 (12.5%) needed treatment (48 endoscopic, 4 vascular embolization, 0 surgery). The most common source bleeding was diverticular 115 (28.3%). The RockMod is better than Strate and Rockall pre-endoscopic for predicting severe bleeding (AUROC 0.85 IC95%(0.81-0.89)) and transfusion (AUROC 0.92 IC95%(0.89-0.95)). GBS and Oakland have AUROC similar to RockMod to predict severe bleeding and need of transfusion. RockMOD is similar to the other four scores to predict re-bleeding and need of treatment. All the risk scores were more accurate for determining need transfusion than severe bleeding. For RockMOD the best cut-off for predicting severe bleeding was ≥ 4 . Sensivity 80.6%, specificity 69.6%, predictive positive value 52.6%, predictive negative value 89.5 % The AUROC curve for each score and outcome are shown in table.

Conclusion: The RockMOD may be an useful tool for risk stratification in acute LGB. RockMOD, GBS and Oakland scores have AUROC similar to predict severe bleeding and need of transfusion. These three scores include the variable hemoglobin in their design.

Score	Severe bleeding *	Transfusion	Treatment	Rebleeding
RockMOD	0.85 (0.81-0.89)	0.92 (0.89-0.95)	0.65 (0.57-0.73)	0.76 (0.69-0.84)
GBS	0.81 (0.76-0.86)	0.89 (0.85-0.92)	0.65 (0.56-0.73)	0.72 (0.64-0.81)
Oakland score	0.89 (0.85-0.93)	0.89 (0.85-0.93)	0.63 (0.55-0.72)	0.75 (0.58-0.75)
Strate	0.70 (0.65-0.75)	0.68 (0.62-0.73)	0.60 (0.52-0.67)	0.68 (0.59-0.76)
Pre-endoscopic Rockall	0.64 (0.68-0.70)	0.70 (0.65-0.76)	0.57 (0.49-0.64)	0.67 (0.58-0.75)

[Table: AUROC and 95%IC for RockMOD AND RISK SCORES. *cut-off severe bleeding ≥ 4 Sensivity 81%, Specificity 70%; PPV 53%, PNV 90 %.]

References: Tapaskar N, Jones B, Mei S, Sengupta N. Comparison of clinical prediction tools and identification of risk factors for adverse outcomes in acute lower GI bleeding. *Gastrointest Endosc.* 2019 May;89(5):1005-1013

Disclosure: Nothing to disclose

P0664

SAFE DISCHARGE IN LOWER GASTROINTESTINAL BLEEDING - IS THE OAKLAND SCORE A GOOD PREDICTOR?

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Introduction: The Oakland score was suggested in 2017 as the first risk stratification score specifically designed for lower gastrointestinal bleeding (LGIB). It includes age, gender, previous admission for LGIB, rectal examination findings, heart rate, systolic blood pressure and hemoglobin concentration, and a score ≤ 8 represents minor bleeding, predicting a 95% probability of safe discharge. Although validated in the United Kingdom, its usefulness in other populations has never been published.

Aims & Methods: Aim: To assess the ability of the Oakland score to predict safe discharge and compare it with other existing scores applied to LGIB.

Methods: Consecutive LGIB admissions to the emergency department over 8 years were retrospectively reviewed. Safe discharge was defined as the absence of rebleeding, blood transfusion, therapeutic intervention, 28-day readmission, or death. The performance of the Oakland score for safe discharge was compared with the BLEED, Strate, NOBLADS and Birmingham scores.

Results: A total of 165 patients were included: 51.5% were men, and the mean age was 71 ± 15 years. Patients had a mean Oakland score of 17 ± 6 , 3.6% with minor bleeding (scores ≤ 8). Safe discharge was identified in 29.7% of patients.

The Oakland score had the greatest discriminative capacity to predict safe discharge (AUC = 0.762; $P < 0.001$), and was better than Birmingham (AUC = 0.758; $P < 0.001$), NOBLADS (AUC = 0.717; $P = 0.01$), Strate (AUC = 0.598; $P = 0.047$) and BLEED scores (AUC = 0.509; $P = 0.88$). In this study, an Oakland score ≤ 8 represents minor bleeding with a 100% safe discharge probability.

Conclusion: The Oakland score is a very useful tool in the context of LGIB, since it allows, with a good discriminative capacity, the identification of patients who can safely be managed in an outpatient setting.

Disclosure: Nothing to disclose

P0665

BIRMINGHAM SCORE: SIMPLIFYING THE PREDICTION OF THE PROGNOSIS IN LOWER GASTROINTESTINAL BLEEDING

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Introduction: Lower gastrointestinal bleeding (LGIB) is common in clinical practice, and a sufficiently robust and consensual risk stratification tool is not yet available. The Birmingham score is a simple tool, that includes only patient's gender and hemoglobin value, ranges from 0 to 7 points, and was developed and validated in 2019 to stratify LGIB outcomes. As a

score < 2 represents a probability of adverse outcomes of 4%, discharge can be considered without further urgent investigation, guiding the hospital admission decision.

Aims & Methods: Aim: To evaluate the ability of the Birmingham score to predict adverse outcomes in LGIB and to compare it with other prognostic scores.

Methods: Retrospective study that included consecutive admissions to the emergency department for LGIB over 8 years. The performance of the Birmingham score to predict adverse outcomes was compared with the BLEED, Strate, NOBLADS and Oakland scores. Adverse outcomes were defined as the composite of blood transfusion, endoscopic and/or surgical intervention, CT angiography, rebleeding or mortality.

Results: We included 165 patients, with a mean Birmingham score of 4.0 ± 2.0 , and 11.5% with a score < 2 . At least one adverse outcome was identified in 68.5% of patients. The Birmingham score showed good discriminative capacity to predict adverse outcomes in LGIB (AUC = 0.758; $P < 0.001$), which was higher than the Oakland (AUC = 0.745; $P < 0.001$), NOBLADS (AUC = 0.717; $P = 0.01$), Strate (AUC = 0.599; $P = 0.048$) and BLEED (AUC = 0.502; $P = 0.97$) scores. A Birmingham score < 2 represented a 5.3% probability of adverse outcomes.

Conclusion: The Birmingham score allows a simple stratification of the risk of adverse outcomes in LGIB, with a performance superior to other scores, thus representing a very practical and useful tool for risk stratification in the context of LGIB.

Disclosure: Nothing to disclose

P0666

RISK STRATIFICATION OF LOWER GASTROINTESTINAL BLEEDING: VALIDATION OF THE OAKLAND SCORE IN A TERTIARY CENTER

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Introduction: Lower gastrointestinal bleeding (LGIB) is associated with less need for endoscopic intervention, hospitalization and mortality when compared to upper gastrointestinal bleeding (UGIB). For this reason, there are no risk stratification scores widely used and validated in LGIB. With this in mind, Oakland score was developed in order to identify the group of patients who can be safely discharged and treated as outpatients.

Aims & Methods: This retrospective work aims to validate Oakland score in a single tertiary hospital.

We included all patients from January to December 2019, submitted to urgent colonoscopy for rectal bleeding (blood/clots per rectum), hematochezia and/or melaena (without UGIB). Patients transferred from other centers, inpatients and patients with UGIB were excluded.

We calculated the Oakland score based on age, sex, previous LGIB, blood on digital rectal exam, hemoglobin level, systolic blood pressure and heart rate. A score value ≤ 8 points was considered, according to the original paper. Safe discharge criteria were defined as the absence of rebleeding, blood transfusion, therapeutic intervention, 28 day readmission, or death. We aimed to evaluate whether this score was predictive of a safe discharge and thereby useful in our clinical practice.

Results: We included 199 patients, 51.8% were males, with an average age of 69.7 ± 16.7 years.

The most common comorbidities were cardiovascular disease (26.1%) and active neoplasias (10.6%). Ischaemic colitis was the most common diagnosis (23.6%), followed by proctologic diseases (19.1%) and diverticular bleeding (14.1%).

According to the defined criteria, 105 (52.8%) patients could be safely

discharged. The average Oakland score was 16.29 (± 7.0) points, while 23 (11.6%) patients scored ≤ 8 points.

In our patients, a cut-off of ≤ 8 points was predictive ($p < 0.001$) of a safe discharge, with a sensitivity, specificity, positive predictive value and negative predictive value of 20.2%, 97.9%, 91.3% and 52.6%, respectively.

Conclusion: We consider the Oakland score as a useful and simple tool, requiring data readily available in clinical practice. In our patients with LGIB it was effective in stratifying risk, identifying those who could have been safely discharged. It should be taken into account in future clinical practice as it may help reduce unnecessary hospital admissions.

Disclosure: Nothing to disclose

P0667

TO STUDY THE LONG TERM EFFICACY, SAFETY AND PREDICTORS OF SUCCESS/COMPLICATIONS OF ARGON PLASMA COAGULATION IN MODERATE TO SEVERE CHRONIC RADIATION PROCTITIS. A SINGLE CENTER PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Radiotherapy is routinely used for pelvic malignancies particularly in gynecological neoplastic diseases. However, it is associated with many complications, like Radiation proctitis which occurs in 1%-5% of patients. Argon plasma coagulation (APC) is currently recommended as the first choice treatment for hemorrhagic CRP, however, its efficacy based on long term follow-up is still unclear. To fill the same gap in literature, this study was done.

Aims & Methods: This was a Prospective observational study of consecutive Chronic radiation proctitis with moderate to severe symptoms who were treated with APC for January 2017 to February 2020. Demographics, clinical variables, and typical endoscopic features were recorded independently every 3 months after treatment completion for a total of two years. Success was defined as either cessation of bleeding, mucous or diarrhoea for at least 12 months after the last APC treatment.

This was a Prospective study of consecutive Chronic radiation proctitis with moderate to severe symptoms who were treated with APC for January 2017 to February 2020. Demographics, clinical variables, and typical endoscopic features were recorded independently every 3 months after treatment completion for a total of two years. Success was defined as either cessation of bleeding, mucous or diarrhoea or only occasional traces of bloody stools with no further treatments for at least 12 months after the last APC treatment.

Results: Four hundred and thirty nine patients with moderate to severe radiation proctitis who failed on medical treatment were included. They were studied for median follow-up period of 28 months (range: 24 to 36 months). Fifteen (24.3%) patients required blood transfusion before APC treatment with $HB \leq 7$ gm/dl. Successful treatment with APC was achieved in 403 (97.1%) of patients. The mean number of APC sessions was 1.6 (1-4). This remission of proctitis was maintained in 343 (78.1%) of patients for a period of 2 years. Multivariate analysis showed that APC failure was independently associated with telangiectasias present more than 10 cms in length and or involving $>60\%$ of the surface area [odds ratio (OR) = 6.53, 95% confidence interval (CI): 1.09- 39.19, $P = 0.04$] and ulcerated area greater than 1.3 cm^2 (OR = 8.15, 95%CI: 1.63- 40.88, $P = 0.01$). Only Six (2.3%) patients had severe adverse events in the form of rectal perforation or rectovaginal fistulization. The only factor significantly associated with severe complications was ulcerated area greater than 1.3 cm^2 ($P = 0.035$).

Conclusion: APC is a very effective and safe treatment option for moder-

ate to severe radiation proctitis on long term basis. Length more than 10 cms, circumference of the telangiectasia $>60\%$ and ulcerated area $>1.3 \text{ cm}^2$ are significantly associated with failure or complications of this treatment.

Disclosure: Nothing to disclose

P0668

OUTCOMES FROM THE UK PURASTAT REGISTRY: A MULTICENTRE OBSERVATIONAL STUDY OF PURASTAT USE IN GASTROINTESTINAL BLEEDING

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Introduction: PuraStat is a novel haemostatic agent without the risk of thermal injury, perforation or loss of mucosal views associated with other treatments such as heat therapy, clips or haemostatic powders.

Aims & Methods: Our aim was to evaluate the efficacy of PuraStat in the prevention and treatment of gastro-intestinal bleeding. We performed a prospective analysis of PuraStat use in the UK, with 6 tertiary referral centres open to recruitment. Data was collected on procedure & lesion details, haemostasis management and complications for endoscopies where PuraStat was used.

Results: 206 procedures were included, consisting of 200 high risk resections (52 EMR, 148 ESD) and 6 upper gastrointestinal bleeds. PuraStat was used for immediate haemostasis in 101 bleeding episodes and for prevention of delayed bleeding in 179 cases (Table 1). Average volume of PuraStat used was 0.43mls for haemostasis and 2.33mls for prevention of delayed bleeding. No PuraStat related complications reported.

Indication	Procedures n=206 (n)	Immediate haemostasis n=101 (n, %)	Prevention of delayed bleeding n=179 (n, %)
High risk resection	200	91/99 (91.9%)	171/175 (97.7%)
Upper gastrointestinal bleed	6	2/2 (100%)	4/4 (100%)
Total	206	93/101 (92.1%)	175/179 (97.8%)

[Haemostatic efficacy of PuraStat]

Conclusion: Our data shows PuraStat is safe and effective for a range of indications, with most use within high risk resections. It shows high efficacy in both immediate haemostasis and prevention of delayed bleeding. We believe PuraStat is a promising new agent in the prevention and management of gastro-intestinal bleeding.

Disclosure: Nothing to disclose

P0669 WITHDRAWN

P0670

USE OF HEMOSPRAY IN THE TREATMENT OF LOWER GASTROINTESTINAL BLEEDS: OUTCOMES FROM THE INTERNATIONAL MULTICENTRE HEMOSPRAY REGISTRY

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Introduction: Lower Gastrointestinal bleeding (LGIB) accounts for approximately 20% of all GI bleeds, with significant mortality in the elderly and those with comorbidities. Common current endoscopic methods for achieving haemostasis include Adrenaline injection, Mechanical clips and thermal therapy. Hemospray (Cook Medical, North Carolina, USA) is a haemostatic powder for GI bleeding. There is a small amount of data on its use in LGIB's. The primary aim was to look at the safety and efficacy of Hemospray in the treatment of LGIBs.

Aims & Methods: Data was prospectively collected on the use of Hemospray in LGIB's in 16 Centres in the USA, UK, Germany, France and Spain (January 2016 - November 2019). Hemospray was used as a monotherapy, combination therapy with standard haemostatic techniques or rescue therapy. Haemostasis was defined as the cessation of bleeding within 5 minutes of application of Hemospray. Rebleeding was defined as a sustained drop in Hb (>2g/l), haematemesis or melaena with haemodynamic instability following index endoscopy.

Results: 24 patients with LGIB's were recruited (16 males, 8 females). The causes of bleeding included malignancy (6/24, 25%), post procedure (polypectomy/ESD) (5/24, 21%), inflammation/angiodysplasia (7/24, 29%), rectal ulcer (3/24, 13%) and oozing polyp (2/24, 8%). The median diameter of lesions was 20mm (IQR, 25-50). 9/24 (38%) of patients were on antiplatelets or anticoagulants.

Overall immediate haemostasis was achieved in 22/24 (92%) of patients. 2/19 (11%) had a re-bleed within 7 days, 4/19 (21%) had a re-bleed within 30 days. 2/21 (10%) died within 30 days (all cause mortality). The two patients that failed treatment had surgery. There was haemostasis rates of 100% in the monotherapy cohort and 88% in the combination therapy cohort (Table 1). In combination Hemospray was always used as a second or third modality. There was a 78% immediate haemostasis rate in patients on antiocoagulants or antiplatelets.

There was no adverse events associated with the use of Hemospray.

Conclusion: These results show that Hemospray is safe and also effective to use in LGIB's with 92% overall haemostasis rates. There are better outcomes when used as a Monotherapy. Anticoagulants/antiplatelets seem to have an effect on haemostasis rates with Hemospray in LGIBs (78% vs 100%). Lower GI bleeds are particularly difficult to treat. Hemospray is an effective alternative in situations where the bleeding point is difficult to access and where there is a large surface of bleeding. Larger randomised trials are required to validate these results.

	Monotherapy (n=15)	Combination (n=8)	Rescue (n=1)
Haemostasis	15/15 (100%)	7/8 (88%)	0/1
Re-bleeding	3/13 (23%)	1/6 (17%)	n/a
7-day mortality	1/13 (8%)	0	0
30-day mortality	2/13 (15%)	0	0

[Table 1. Outcomes in the Hemospray treatment subgroups]

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P0671

ASSOCIATION OF HYSTOLOGIC SUBTYPES AND HIGH-RISK SERRATED POLYPS WITH SYNCHRONOUS COLORECTAL CANCER: A COMMUNITY-BASED STUDY

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Introduction: Serrated polyps (SP), which include hyperplastic polyps (HP), sessile serrated adenomas/polyps (SSA/P) and traditional serrated adenomas (TSA)), are considered premalignant lesions, but their association with synchronous colorectal cancer (sCRC) is not well known.

Some features of SP are associated with increased risk of metachronous advanced colorectal lesion, specially SP ≥ 10 mm or SP with dysplasia (SPwD), considering these lesions as high-risk serrated polyps (HRSP).

Aims & Methods: The aim of this study was to evaluate the association of the different histological subtypes of SP and HRSP with sCRC. A large, prospective crosssectional multicenter, community-based study was conducted involving 8530 patients prospectively collected who underwent colonoscopy according to routine clinical practice between January 1 and December 31, 2011.

Results: Multivariate analysis associated the presence of TSA or SSA/P with increased risk of sCRC (OR, 3.15; 95%CI: 1.42 - 6.99 and OR, 2.03; 95%CI, 1.27 - 3.24 respectively). According to the location of sCRC, the presence of TSA or SSA/P was associated only with the presence of proximal sCRC. The presence of at least one HRSP was associated with increased risk of sCRC (OR 2.81, 95%CI 1.68 - 4.71; p<0.001), specially with proximal location (OR 3.72, 95%CI 1.91 - 7.23; p<0.001).

We also found that the presence of at least one proximal SP or >2 SSA/P were associated with sCRC (OR 2.12, 95%CI 1.47 - 3.06; p < 0.001 and OR 4.34, 95%CI 1.14 - 13.14; p=0.01 respectively). The prevalence of serrated poliposis syndrome in our poblational study was 0.18%.

Conclusion: The presence of TSA, SSA/P, HRSP, proximal SP as well as multiple SSA/P was associated with increased risk of sCRC, particularly with proximal location of sCRC and therefore, these features of SP should be considered as a marker of risk of sCRC.

Disclosure: Nothing to disclose

P0672

THE EFFECTIVENESS OF THE STANDARDIZED COURSE OF CARE - IDENTIFICATION OF COLORECTAL CANCER IN THE ÖREBRO REGION, SWEDEN

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Introduction: To shorten time to diagnosis in patients with suspected colorectal cancer (CRC), a number of countries have introduced standardized cancer patient pathways (CPP). In 2016, CRC was introduced to the Swedish CPP, called standardized course of care (SCC). If a patient fulfills one or more of the entry criteria for the SCC-CRC, a colonoscopy should be performed within 10 days to investigate whether the patient has CRC. Inevitably, the SCC targets increases the burden on endoscopy resources. Furthermore, it is unknown whether the Swedish SCC-CRC leads to a better outcome for patients.

Aims & Methods: We performed a retrospective cohort study of patients diagnosed with CRC found through colonoscopy in the Örebro Region between September 2016, and December 2018. We aimed to investigate whether there is a difference between CRC found via SCC-CRC and the routine waiting list (non-SCC-CRC). Outcome measures comprised: time to diagnosis, disease stage (TNM I-IV and tumor grade), tumor location and indications for referral, which were collected from patient journals. The route by which patients were presented was categorized as within the SCC (CRC-SCC) or routine waiting list (non-CRC-SCC). Diagnostic interval (DI) was defined as days between the referral and the colonoscopy. Chi2-tests for bivariate data and Mann-Whitney U tests for non-normally distributed continuous and ordinal data were performed to compare both groups.

Patient characteristics	SCC-CRC group (n=217)	Non-SCC-CRC group (n=130)	Missing cases (%) SCC-CRC group/ non-SCC-CRC group	P-value
Diagnostic interval, median (IQR)	13.0 (8.0-17)	21.5 (7.0-43)	0/0	<.001*
Tumor stage I-IV, mean (SD)	2.5 (1.1)	2.4 (1.1)	0/0.8	.18
Low differentiated cancer, n (%)	37 (19.4)	20 (17.9)	12/14	.75
Hemoglobin value (g/L), median (IQR)	117 (102-136)	106 (87-129)	9.7/8.5	.001*
Bleeding anemia, n (%)	60 (52.8)	74 (69.2)	32/18	<.001*
Rectal cancer, n (%)	92 (42.4)	24 (18.5)	0/0	<.001*
Meeting any SCC-criteria, n (%)	205 (94.5)	108 (83.1)	0/0	.001*
Meeting any SCC-criteria, excluding bleeding anemia n (%)	176 (81.1)	57 (43.8)	0/0	<.001*

[The different characteristics of the CRC patients included in the standardized course of care (SCC-CRC) and routine waiting list (non-SCC-CRC).]

Results: 62.5% of the patients who were diagnosed with CRC through colonoscopy were referred according to the SCC-CRC and 37.5% of the patients were diagnosed via the non-SCC-CRC. No difference in tumor stage or tumor grade was observed between the two groups. The non-SCC-CRC showed a longer time to diagnosis than the SCC-CRC group (21.5 days, IQR 7-43 vs. 13 days, IQR 8-17, $p < .001$, respectively). In the SCC-CRC group,

there were significantly more rectal cancers (42.4% vs. 18.5%, $p < .001$). The non-SCC-CRC group showed significantly more bleeding anemia (69.2% vs. 52.8%, $p < .001$) and a lower median hemoglobin value (106 g/L IQR 87-129 vs. 117 g/L, IQR 102-136, $p = .001$). Surprisingly, 83% of the non-SCC-CRC patients met one or more of the SCC-CRC referral criteria, with bleeding anemia of unknown cause as the most common criterion.

Conclusion: Our results suggest that the risk for CRC in patients with bleeding anemia may be underestimated by physicians. As a result, a significant proportion of these patients are not included in the SCC-CRC. The SCC-CRC seems to be more sensitive for diagnosing rectal cancer. Furthermore, the SCC-CRC appears to be of value in shortening time to diagnosis. However, both groups were investigated reasonably fast after the date of referral and this explains why there is no significant difference in the outcome with respect to tumor stage or prognosis. Our findings suggest that larger studies evaluating the SCC-CRC are needed in order to establish the benefits of the SCC-CRC.

Disclosure: Nothing to disclose

P0673

CARDIORESPIRATORY FITNESS (CRF) AND COLORECTAL CANCER (CRC) INCIDENCE AND MORTALITY: A SYSTEMATIC REVIEW

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Introduction: Cardiorespiratory fitness (CRF) predicts overall health and cardiovascular disease. Colorectal cancer (CRC) shares several common risk factors with cardiovascular disease including physical inactivity. CRF, as determined by an exercise test, represents an objective, reproducible measure of the functional consequences of physical activity.

Aims & Methods: The aim is to summarize the evidence linking CRF, as measured by exercise testing, with CRC incidence and mortality and colorectal adenoma incidence. The databases searched include MEDLINE, EMBASE and PsycINFO during the period from inception until July 2018. Cohort and case control studies that measured CRF by exercise testing and reported outcomes on CRC or colorectal adenoma incidence, or CRC related mortality were selected using predefined eligibility criteria.

One reviewer abstracted the study data, and another reviewer verified it. Two reviewers graded risk of bias independently. Discrepancies were resolved by a third reviewer. The study quality was assessed using a critical appraisal tool adapted from Dans et al (Ref). The studies were appraised for directness and validity of the reported results.

Results: A total 1580 unique articles were screened. Ten studies (130 957 subjects) met eligibility criteria. All 10 studies were prospective cohort studies (Table). There was a trend for high CRF to be associated with CRC incidence and mortality. There were no studies on the association between CRF and adenoma. An overall meta-analysis could not be performed because of heterogeneous definitions of outcomes. Also, the included studies were of moderate quality.

Conclusion: There is insufficient evidence to support an association between CRF and CRC incidence, CRC mortality and colorectal adenoma. Future research should address shortcomings in existing studies.

References: Dans AL, Dans LF, Silvestre MAA. Painless evidence-based medicine: John Wiley & Sons, 2016.

Disclosure: Nothing to disclose

Study ID	Setting	Sample Size	Duration of follow-up	Patient Characteristics	Exposure (CRF)	Reported Outcome(s)	CRF classification	Reported Outcomes	Risk of Bias
Lakoski 2015	CCLS, USA	13949	mean of 6.5 years	Participants undergoing a preventive health examination Mean (SD) age in years: 49 (9) Mean (SD) CRF in METs: 11.0 (2.3)	Incremental treadmill test (Modified Balke protocol). CRF was quantified using peak METs.	1. CRC incidence 2. All-cause mortality and cause-specific mortality among men who developed cancer at Medicare age (65 years and above).	Three groups: low (lowest 20%), moderate (middle 40%) and high (upper 40%).	1. CRC incidence: adjusted HRs for CRC incidence (using low CRF as reference category) moderate CRF group - 0.67 (95% CI, 0.46-0.98) high CRF group - 0.56 (95% CI, 0.36-0.87 2. Cancer mortality in men diagnosed as having lung, colorectal, or prostate cancer; adjusted HRs for cancer mortality (using low CRF as reference category) high CRF group- 0.68 (95% CI, 0.47-0.98)	Low
Vainshelboim 2017a	USA	4920	12.7 years (mean)	Participants undergoing exercise testing for clinical reason	Treadmill protocol. CRF was estimated using peak METs.	Overall cancer incidence	Three groups: low (< 5METs) , moderate (5-10 METs), high (< 10 METs)	Overall cancer incidence: adjusted HR (low CRF as reference category) CRC incidence : adjusted HR	Some concern
Peel 2009	ACLS, USA	38801	17 years (mean)	Participants undergoing a preventive health examination Mean (SD) age in years: 43.8 (9.7) Mean (SD) CRF in METs: 11.6 (2.5)	Incremental treadmill test (Modified Balke protocol). CRF was quantified using peak METs.	Digestive cancer mortality including CRC mortality	Three groups: low (lowest 20%), moderate (middle 40%) and high (upper 40%).	CRC mortality adjusted RR for CRC mortality in the fit group (unfit group as reference) 0.58 (95% CI, 0.37-0.92)	Low
Farrell 2007	ACLS, USA	38410	17.2 years (mean)	Participants undergoing a preventive health examination Mean (SD) age in years: 43.8 (9.9) Mean (SD) CRF in METs: 12.2 (2.5)	Incremental treadmill test (modified Balke protocol). CRF was quantified using peak METs.	Cancer mortality	Quintiles: Quintile 1 (<9.9 METs) Quintile 2 (9.9 to 10.8 METs) Quintile 3 (10.9 to 12.6 METs) Quintile 4 (12.7 to 14.0 METs) Quintile 5 (>14.0 METs)	Cancer mortality Adjusted HRs (lowest CRF, Quintile 1 as reference) Quintile 2 - 0.71 (95% CI, 0.60-0.85) Quintile 3 - 0.69 (95% CI, 0.58-0.83) Quintile 4 - 0.73 (95% CI, 0.61-0.89) Quintile 5 - 0.53 (95% CI, 0.43-0.67)	Low
Farrell 2011	ACLS, USA	14256	15.2 years (mean)	Participants undergoing a preventive health examination Mean (SD) age in years: 43.8 (10.2) Mean (SD) CRF in METs: 9.5 (2.1)	Incremental treadmill test (modified Balke protocol). CRF was quantified using peak METs.	Cancer mortality	Three groups: low (quintile 1), moderate (quintiles 2-3) high (quintiles 4-5).	Cancer mortality Adjusted HRs for cancer mortality (low CRF as reference) moderate CRF - 0.89 (95% CI, 0.67-1.18) high CRF - 0.68 (95% CI, 0.47-0.97)	Low
Evenson 2003	LRC, USA	5475	24.9 years (median)	Community-based participants undergoing health examination Men Mean (SD) age in years: 46.7 (11.3) Mean (SD) exercise test duration in minutes: 9.5 (2.3) Women Mean (SD) age in years: 45.1 (10.3) Mean (SD) exercise test duration in minutes: 7.3 (2.3)	Incremental treadmill test (Bruce protocol). CRF was quantified as the duration of the exercise test in minutes.	Overall cancer mortality	Quintiles: Quintile 1 (lowest CRF) to Quintile 5 (highest CRF).	1. Cancer mortality in men; Adjusted HRs for cancer mortality (Quintile 1 as reference) Quintile 2 - 1.02 (95% CI, 0.67-1.54) Quintile 3 - 0.90 (95% CI, 0.61-1.32) Quintile 4 - 0.91 (95% CI, 0.63-1.33) Quintile 5 - 0.41 (95% CI, 0.23-0.75) 2. Cancer mortality in women Adjusted HRs for cancer mortality (Quintile 1) as reference Quintile 2 - 1.09 (95% CI, 0.71-1.68) Quintile 3 - 1.04 (95% CI, 0.67-1.62) Quintile 4 - 0.89 (95% CI, 0.55-1.43) Quintile 5 - 0.82 (95% CI, 0.47-1.43) 3. Cancer mortality in participants with the lowest CRF (Quintile 1) Adjusted HRs for cancer mortality (participants in Quintiles 2-5 as reference) Men - 1.11 (95% CI, 0.82-1.51) Women - 1.01 (95% CI, 0.71-1.43) 4. Cancer mortality in participants with the highest CRF (Quintile 5); Adjusted HRs for cancer mortality (participants in Quintiles 1-4 as reference) Men - 0.47 (95% CI, 0.27-0.81) Women - 0.84 (95% CI, 0.52-1.36)	Some concern
Sawada 2003	Japan	9039	16 years (mean)	Participants undergoing a workplace health examination Survivors Mean (SD) age in years: 35.8 (9.1) Mean (SD) VO2max in mL/(kg·min): 37.1 (6.9) Deceaseds Mean (SD) age in years: 45.8 (9.2) Mean (SD) VO2max in mL/(kg·min): 33.3 (6.6)	Incremental cycle ergometer. VO2max was estimated using Åstrand-Rhyming Nomogram and Åstrand's Nomogram correction factors	Overall cancer mortality	Quartiles: Quartile 1 (lowest CRF) to Quartile 4 (highest CRF).	Cancer mortality Adjusted RRs for cancer mortality (Quartile 1 as reference) Quartile 2 - 0.75 (95% CI, 0.48-1.16) Quartile 3 - 0.43 (95% CI, 0.25-0.74) Quartile 4 - 0.41 (95% CI, 0.23-0.74)	Some concern
Robsham 2017	Norway	1997	26.2 years (mean)	Males undergoing health screening	Incremental bicycle exercise test. CRF was measured as total work performed in the bicycle test divided by body weight(kJ/kg)	CRC incidence	Tertile : 1: <118.9 (mean 91.9) Tertile 2: 119-161.4 (mean 139.1) Tertile 3: >161.5 (mean 207.9)	Adjusted HR for site-specific cancer incidence Colon cancer : Tertile 1 - HR : 1.00 (Reference) Tertile 2 - HR : 0.60 (95% CI, 0.35, 1.01) Tertile 3 - HR : 0.69 (95% CI, 0.40, 1.17) Rectal cancer(Reference) Tertile 1 HR : 1.00 Tertile 2 HR : 1.65 (95% CI, 0.76, 3.61) Tertile 3HR : 1.16 (95% CI, 0.49,2.73)	Low
Sawada 2014	Japan	8760	20.2 years (mean)	Participants undergoing a workplace health examination	Submaximal cycle ergometer. VO2max was estimated using Åstrand-Rhyming Nomogram and Åstrand's Nomogram correction factors. (mL·kg ⁻¹ ·min ⁻¹)	Cancer mortality	Tertiles (mean ±SD) Low fitness(30.2 ± 3.4) Moderate fitness(36.1 ± 2.9) High fitness (44.0 ± 5.4)	Cancer mortality Multivariable adjusted HR Low fitness- 1.00 (Reference) Moderate fitness- 0.70 (95% CI, 0.39,1.27) High fitness -0.47 (95% CI, 0.23, 0.97)	Some concern
Vainshelboim 2017b	USA	5876	9.9 years (mean)	Participants undergoing exercise testing for clinical reason	Treadmill protocol. CRF was estimated using peak METs.	Overall cancer mortality	Quartiles Quartile 1: < 5 METs Quartile 2: 5 to <8 METs Quartile 3: 8 to <10 METs Quartile 4: ≥10METs	Cancer mortality Quartile 1 risk reduction: (Reference) Quartile 2 risk reduction : 26% (95% CI, 0.6-0.92) Quartile 3 risk reduction: 40% (95% CI, 0.42-0.85) Quartile 4 risk reduction : 46% reduced risk (95% CI, 0.36 -0.82)	Some concern

[P0673 Table. Characteristics of studies included in this systematic review and their reported outcomes]

P0674

SOCIOFAMILIAR VARIABLES ASSOCIATED WITH THE ADHERENCE TO A COLORECTAL CANCER POPULATION SCREENING PROGRAM

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Introduction: High participation in colorectal cancer (CRC) screening programs is the key to the effectiveness of its preventive effect. Although it is recommended to reach 65%, in Spain it is around 58%. Sociofamiliar support is known to be a protective variable in several diseases.

Aims & Methods: The aim of this study is to analyze the effect of sociofamiliar support in the participation of CRC population screening program. We designed a multicentric case (n=248)-control (n=194) study. We perform the study in three Primary Healthcare Clinics in the city of Valencia, Spain, between March and September of 2019. Individuals participating in the CRC screening program were considered cases. Data from demographic characteristics, type of family, social network, social support (social support scale MOS), familiar function, quality of life (EuroQol questionnaire) and the existence of stressful life events (SLE) were collected. Variables that showed statistical significance in a bivariate analysis were introduced in a logistic regression model.

Results: Mean age was 59.4 ± 5.2 years, 54.8% were women, 72.1% lived with their stable couple and 75.1% had a nuclear family. Mean number of social contacts was 10.3 ± 7.8, 31.4% had small or medium social networks (<5 social contacts), 19.9% had high impact SLE, 23.9% were feeling anxious or depressed and 78.9% claimed that the important family decisions were taken in group. We detected a statistical significant association between the adherence to the CRC screening and the age (cases = 60.33, controls = 58.33 years; OR = 1.08, 95% CI = 1.04-1.12), a stable couple (cases = 78.6%, controls = 63.2%; OR = 2.14; 95% CI = 1.38-3.32), a nuclear family (cases = 79.8%, controls = 68.4%; OR = 1.73; 95% CI = 1.09-2.72), a wide social network (cases = 74.3%, controls = 60.8%; OR = 1.86, 95% CI = 1.22-2.84), feeling anxious or depressed (cases = 20.2%, controls = 29.2%; OR = 0.61, 95% CI = 0.38-0.96), having someone that takes you to the doctor appointments when needed (cases = 77.6%, controls = 63.5%; OR = 2.68, 95% CI = 1.21-5.98) and high impact SLE (cases = 15.2%, controls = 26.5%; OR = 0.49, 95% CI = 0.30-0.81). In the multivariate analysis, we identified an independent association between the adherence and the age (OR = 1.05, 95% CI = 1.01-1.1), a stable couple (OR = 1.82, 95% CI = 1.15-2.88), a wide social network (OR = 1.71, 95% CI = 1.1-2.66) and having someone that takes you to the doctor appointments when needed (OR = 1.59, 95% CI = 1.01- 2.66).

Conclusion: We detected an independent association between the participation in CRC population screening programs and several sociofamiliar variables that should be taken into consideration in the strategies aimed at increasing the adherence.

Disclosure: Nothing to disclose

P0675

PREDICTIVE VALUE OF CARCINOEMBRYONIC ANTIGEN IN SYMPTOMATIC PATIENTS WITHOUT COLORECTAL CANCER. POST-HOC ANALYSIS WITHIN COLONPREDICT COHORT

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Introduction: Serum carcinoembryonic antigen (CEA) is mainly used as a prognostic biomarker for monitoring recurrence of colorectal cancer (CRC) following curative resection. The clinical value of CEA for the assessment of patients presenting abdominal symptoms is unknown.

Aims & Methods: We aim to assess the incidence of various types of cancer and its related death in symptomatic patients without colorectal cancer (CRC) in a complete baseline colonoscopy.

Post-hoc retrospective cohort analysis performed within COLONPREDICT study, a diagnostic accuracy study evaluating faecal immunochemical test in symptomatic patients.[1] Symptomatic patients without CRC in a complete basal colonoscopy were divided into two groups (CEA ≤/ > 3 ng/dL) and data from follow-up were retrieved from electronic medical records. For all patients, cancer diagnoses of any aetiology and death were recorded. Hazard rates (HR) were calculated adjusting by age, sex and presence of advanced adenoma. Finally, we analysed which variables were independently associated with the detection of any malignancy during the first year.

Results: We analysed 1431 patients, 238 (16.6%) with CEA > 3 ng/dL. Patients with CEA > 3 ng/dL were older (64.7 vs 67.4 years old; *p* 0.005). There were no differences (*p* > 0.05) between both cohorts in gender, prevalence of abdominal symptoms or basal colonoscopy findings (significant colonic lesion). Over 36.5±8.4 months, 30 (2.1%) developed gastrointestinal cancer (GIC) (upper GIC:22, CRC:8) and 85 patients (5.9%) were diagnosed with cancer located outside from the gastrointestinal (GI) tract. Subjects with high CEA levels showed higher CRC (HR 4.4, 95% confidence interval-CI 1.1-17.7) and non GIC risk (HR 1.7, 95% CI 1.0-2.8) with no differences in upper GIC risk (HR 2.2, 95% CI 0.9-5.4). One hundred (7.0%) patients died during the follow up. 41 (2.9%) due to non-cancer causes. Twenty-one (1.5%) patients died from GIC. Of these, 6 (0.4%) were CRC related. Thirty-eight (2.7%) patients died from cancer located outside the GI tract. Subjects with high CEA levels showed higher risk of death due to CRC (HR 8.8, 95% CI 1.6-48.5) and non-gastrointestinal cancer (HR 3.5, 95% CI 1.8-6.7). Again, there were no differences in upper GIC risk (HR 2.3, 95% CI 0.8-6.8). A new malignancy was detected in 51 (3.6%) patients during the first year. Three variables were independently associated: anaemia (OR 2.8, 95% CI 1.3-5.8), rectal bleeding (OR 0.3, 95% CI 0.1-0.7) and CEA level > 3 ng/dL (OR 3.4, 95% CI 1.7-7.1).

Conclusion: Symptomatic patients without CRC in a complete basal colonoscopy and CEA level > 3 ng/dL have a moderate increase in the risk of cancer detection for the first year. Anaemia and lack of rectal bleeding independently increased this risk in our cohort.

References: [1] Cubiella J, Vega P, Salve M, et al. Development and external validation of a faecal immunochemical test-based prediction model for colorectal cancer detection in symptomatic patients. *BMC Med* 2016;14:128. DOI: 10.1186/s12916-016-0668-5

Disclosure: Nothing to disclose

P0676

PROGNOSIS OF PATIENTS WITH MULTIPLE COLORECTAL CARCINOMAS: SYNCHRONOUS VERSUS METACHRONOUS MAKES THE DIFFERENCE

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Introduction: Due to its high incidence, colorectal cancer is well characterized. However, only few data exist regarding multiple colorectal cancers in one individual patient.

Aims & Methods: This retrospective observational trial analyses clinical, histological, and molecular pathological characteristics of patients with multiple synchronous and metachronous colorectal cancer. All patients who underwent surgery for colorectal cancer at our university hospital between 1982 and 2019 were assessed.

The primary endpoint was cause-specific survival. Secondary endpoints were recurrence-free survival and group comparisons.

Results: Overall, 3714 patients were included in this analysis. Of those, 3506 had a primary unifocal colorectal cancer, 103 had multiple synchronous carcinomas, and 105 had a metachronous carcinoma.

Multiple synchronous carcinomas occurred more frequently in elderly patients

($p=0.009$) and in male ($p=0.027$). There were no relevant differences concerning

histopathology. Patients with multiple synchronous colorectal cancers did not show altered recurrence or survival rates. Compared to classical unifocal tumors, metachronous colorectal cancers had a lower rate of recurrence (24% vs. 41%, $p=0.002$) and a lower rate of cause-specific death (13% vs. 37%, $p<0.001$). Two-year cause-specific survival rates were $78\pm1\%$ for classical unifocal carcinomas, $73\pm5\%$ for multiple synchronous carcinomas ($p=0.588$), and $94\pm3\%$ for metachronous carcinomas ($p<0.001$).

Upon multivariable analysis, metachronous tumors were an independent favorable prognostic parameter regarding case-specific survival.

Conclusion: Patients with synchronous multiple colorectal carcinomas did not have a reduced prognosis compared to patients with classical unifocal carcinoma. Of interest, metachronous carcinomas in patients who have already had colorectal cancer before, were accompanied by better survival rates in this retrospective analysis.

Disclosure: Nothing to disclose

P0677

IMPORTANCE OF METABOLIC SYNDROME IN COLORECTAL NEOPLASIA OUTCOMES: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Metabolic syndrome (MetS) is a cluster of factors including hyperglycaemia, hypertension, obesity, hyperlipidaemia and hypercholesterolaemia. It has been suggested that MetS increases the risk of colorectal neoplasia and colorectal cancer (CRC) mortality among general population. This systematic review aimed to examine the association of MetS with 1) recurrent colorectal adenoma or occurrent CRC after adenoma resection 2) CRC-related post-surgical complications 3) CRC survival including overall survival (OS), cancer-specific survival (CSS) and progression-free survival (PFS).

Aims & Methods: The review was conducted according to PRISMA guidelines. MEDLINE, Embase, Scopus and Web of Science were searched up to 22.11.2019. Eligible studies with extractable hazard ratios (HR) or odds ratios (OR) were included in meta-analyses (where ≥ 3 studies were available on a specific outcome) using random effects models. I^2 -test was used to assess between-study heterogeneity. Quality appraisal was undertaken with Newcastle-Ottawa score.

Results: 1108 non-duplicate articles were identified with 61 selected for full text assessment: 20 were eligible and included. These articles used different definitions of MetS: 8 AHA or NCEP ATP III or IDF, 5 modified AHA or ATP III, 5 Chinese Diabetes Society, 2 three of four MetS components. Two articles reported an insignificant association between MetS and recurrent adenoma. Two articles combined adenoma and CRC as an overall outcome, one found no association between the two, and another reported an increased risk of adenoma/CRC occurrence with MetS (HR=1.3, 95%CI 1.02-1.73). One article reported a significant association between MetS and recurrent nonadvanced adenoma (OR=1.52, 95%CI 1.08-2.13) only in women and null associations with neoplasia (which included adenoma and CRC) in both sexes. Five articles reported post-surgical complications in CRC patients: 4 assessed CRC-related post-surgical complications (pooled OR=2.76, 95%CI 0.94-8.15, $I^2=93.4$, $n=3$) and 1 combined CRC-related and other post-surgical complications. Ten articles assessed the survival in CRC patients. MetS was statistically significantly associated with CSS (pooled HR=1.80, 95%CI 1.04-3.12, $I^2=92.7$, $n=3$) but was not with OS (1.04, 95%CI 0.94-1.15, $I^2=43.7$, $n=7$) or PFS (1.12, 95%CI 0.89-1.42, $I^2=85.6$, $n=3$). Between-study heterogeneity was insignificantly modest in OS studies.

Conclusion: Our findings suggest that MetS is associated with worse CSS but not with OS, PFS or cancer-related post-surgical complications in CRC patients. Studies on recurrent adenoma or occurrent CRC post adenoma resection are limited. Varying definitions of MetS made comparison of studies difficult and a standardised definition should be developed. Well-designed research is required to better understand the association of outcomes between MetS and colorectal neoplasia.

Disclosure: Nothing to disclose

P0678

COLONOSCOPIST PERFORMANCE AND COLORECTAL CANCER RISK AFTER ADENOMA REMOVAL TO STRATIFY SURVEILLANCE

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Introduction: Colonoscopy surveillance after adenoma removal is an increasing burden in many countries. Surveillance recommendations consider characteristics of removed adenomas, but not colonoscopist performance.

Aims & Methods: We investigated the impact of colonoscopist performance on colorectal cancer risk after adenoma removal. We compared colorectal cancer risk after removal of high-risk adenomas, low-risk adenomas, and after negative colonoscopy for all colonoscopies performed by colonoscopists with low versus high performance quality (adenoma detection rate < 20% versus ≥20%) in the Polish screening program between 2000 and 2011, with follow-up until 2017. Findings were validated in the Austrian colonoscopy screening program.

Results: 173,288 Polish colonoscopies were included in the study. Of 262 colonoscopists, 160 (61.1%) were low performers, and 102 (38.9%) were high performers. 11.1% of individuals had low-risk and 6.6% had high-risk adenomas removed at screening; 82.2% had no adenomas. During 10 years follow-up, 443 colorectal cancers were diagnosed. For low-risk adenoma individuals, colorectal cancer incidence was 0.47% (95%CI 0.33-0.64) with low-performing colonoscopists versus 0.19% (95%CI 0.12-0.29) with high-performing colonoscopists (HR 2.35; 95%CI 1.31-4.21; p=0.004). For high-risk adenoma individuals, colorectal cancer incidence was 0.99% (95%CI 0.75-1.28) with low-performing colonoscopists versus 0.34% (95%CI 0.21-0.54) with high-performing colonoscopists (HR 2.69; 95%CI 1.62-4.47; p< 0.001). After negative colonoscopy, colorectal cancer incidence was 0.27% (95%CI 0.23-0.30) for individuals examined by low-performing colonoscopists, versus 0.12% (95%CI 0.09-0.15) for high-performing (HR 2.10; 95%CI 1.52-2.91; p< 0.001). The findings were confirmed in the Austrian cohort.

Conclusion: Our results indicate that endoscopist performance may be more important than polyp characteristics in determining colorectal cancer risk after colonoscopy screening.

Disclosure: Nothing to disclose

P0679

WHAT ABOUT INTERVAL CANCER? THE EXPERIENCE OF A PORTUGUESE REFERENCE CENTER

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Introduction: Colorectal cancer (CRC) is one of the most common malignancies in the world, with increasing incidence in the developing countries. Therefore, colonoscopy has been widely accepted as the best method of screening and detecting neoplasm in the bowel. Studies show that the incidence of interval CRC is increasing and, in the future, will be more frequent and common than ever.

Aims & Methods: This retrospective study was designed to identify characteristics and risk factors for interval CRC. Medical records of individuals who were newly diagnosed with CRC between January 2018 and December 2019 were reviewed. Their previous endoscopic findings, family history of CRC, diabetes, body mass index (BMI), cigarette smoking, alcohol consumption, cholecystectomy in the past and the need for surgery, chemotherapy or radiotherapy as treatment option were analyzed. Those with the diagnosis of CRC between two consecutive colonoscopies performed within the appropriated surveillance range were considered to have interval CRC.

Results: During the study period, 491 patients were newly diagnosed with CRC. Among them, 61 (12.4%) patients had interval CRC, with median of 52 months (Interquartile range: 39-81,8) between colonoscopies (57.4% patients with a previous normal colonoscopy). Being a referral hospital, it receives patients from many residential areas, with 54.1% of patients of interval group living in rural environments vs 49.1% in the other group, however, in the statistical analysis the rural environment was not a major factor for the emergence of interval cancer.

The age of diagnosis tended to be higher in the study group, with mean age of 70.1 years (vs 68.4 years) and a higher percentage of obese or overweight patient was observed in interval group (69.5% vs 61%), yet their mean BMI tend to be lower (28.6 vs 29.4 Kg/m²).

Interval CRC was more commonly located at right colon (25.3% vs 37.7%; p=0,017) and more frequent in patients with first-degree relatives with CRC (9.2 vs 18%; p=0,031). When comparing the rate of previous cholecystectomy, the interval group has higher rates (11.5% vs 5.5%; p=0,031). Still, they more often have surgery as a therapeutic option (82% vs 71.3%; p=0,049), but the percentage of patients undergoing chemotherapy and/or radiotherapy is similar between the groups. Despite the short period of follow-up, the mortality rate is significantly lower in the interval group (14.8% vs 1.6%; p< 0,001).

In a multivariable analysis, interval cancer was highly related with family history (in a first relative) of CRC (OR, 2.79; 95% CI: 1.23-6.37; p=0,015) and location in the right colon (OR, 3.09; 95% CI: 1.51 - 6.32; p=0,02).

Conclusion: Interval CRC tends to occur more frequently in the right colon and in patient with a family history (in a first relative) of CRC. It is surprising how short the median between colonoscopies is (just 52 months) with a significantly proportion of patient with a normal previous colonoscopy (screening guidelines suggest a new colonoscopy within 10 years and in the most recent guidelines, endoscopic findings involving a 10-year interval have been extended).

This study shows the importance of the interval cancer and the growing need for quality in the index colonoscopy, since the prevalence of CRC is increasing and with it, interval cancer will certainly increase. More studies are needed, preferably prospective and multicentric in order to detect more correctly in which patients the time between screening colonoscopies should be reduced.

Disclosure: Nothing to disclose

P0680

INCIDENCE OF COLORECTAL NEOPLASIA AMONG YOUNG PATIENTS WITH LYNCH SYNDROME IN CORRELATION WITH THE TYPE OF MUTATION. RESULTS OF THE LARGEST PARIS AREA COHORT

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Introduction: International guidelines recommend colorectal cancer (CRC) screening in patients with Lynch Syndrome, starting from 20-25 years-old except for MSH6 and PMS2 where the screening should start at 35 years-old.

Aims & Methods: This is an observational analytical study. All consecutive patients under 50 years-old followed within the PRED-IdF network with a proven germline mutation were included between 2010 and 2019. Demographics, type of mutation and endoscopic data were collected. To assess the age of primary colorectal event, we defined "colorectal neoplasia" (CN) as the detection of any of the following events: CRC, adenoma and/or sessile serrated lesion (SSL). Factors associated to CN were assessed by Cox regression survival analysis.

Results: Seventy-hundred and eight patients (median age: 35 (15-50) years, male ratio 0.7) underwent 2429 colonoscopies during a median follow-up of 55 (0-350) months. They presented with the following mutations: MLH1 (33.5%), MSH2 (45.6%), MSH6 (15.3%), PMS2 (4.2%) and EP-CAM (1.4%).

The quality of colonoscopy preparation was good in 73.5% of cases. Chromo-endoscopy by indigo carmin was performed in 72.7% of cases. The global incidence of CN, CRC, adenoma and SSL were respectively of 53%, 22.9%, 37.9% and 6.6%. For patients with MSH6 mutation, the age at first CN was significantly older than for other mutations (p=0.038). Among these, we reported that 25% of CN occurred before 35 years-old, including 7 adenomas, 1 advanced adenoma, 1 serrated adenoma and 5 CRC.

Overall, by multivariable analysis, age (HR: 1.038, CI95%: 1.026-1.116), male sex (HR: 1.460, CI95% [1.017-1.061]), and tobacco use (HR: 1.672 CI95%: 1.252-2.233), were associated with a higher incidence of CN.

Conclusion: MSH6 mutation and demographic factors were associated with a delayed CN development. However, we report CN in MSH6 carriers before the age of 35 years, which may limit the application of recent guidelines.

Disclosure: Nothing to disclose

P0681

LYNCH SYNDROME - BEYOND THE COLON

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Introduction: Patients with Lynch Syndrome (LS) are at increased risk of multiple cancers. Upper urinary tract tumours have been diagnosed more frequently, particularly in MSH2 mutation carriers. The association between LS and urinary bladder or prostate cancers is still controversial.

Aims & Methods: Our aim was to characterize the tumour prevalence in LS and to evaluate the occurrence of upper urinary tract, bladder and prostate cancers in our population. We included LS families followed in a Familial Cancer Risk Clinic of a specialized centre between 1996 and 2019. Demographic data, gene mutations and tumour diagnosis were evaluated.

Results: A total of 155 families/491 individuals (57.4% females) were included. Mutations in MSH2, MLH1, MSH6, PMS2 genes were identified in 52%, 33%, 12.8% and 1.2% of the patients, respectively. 55% of the patients had a cancer diagnosis (total number of cancers: 453). The mean number of tumours per patient was 1.68 and the mean age at first tumour diagnosis was 45±11 years. The prevalence of urothelial cancers was 4.5% (n=22); they were the first diagnosed tumour in 8 patients; 52.4% of the patients were female and the mean age was 41±16 years; cancers were identified in the ureters (41%), renal pelvis (27%), kidney (9%) and bladder (18%).

Patients with urothelial cancers had family history of these tumours in 90.9% of the cases (19% of patients with family history had urothelial cancers vs 0.5% of patients with no family history, p<0.001). The diagnosis was based on screening in at least 32% of the patients (unknown motif in 10 patients).

Recurrence rate was 14% (n=3) and a second urothelial tumour was found in 24% (n=5). MSH2 mutation carriers demonstrated a significantly higher proportion of urinary tract cancers compared with non-MSH2 mutation carriers (8% vs 0.9%, p<0.001).

Prostate tumours were found in 4% of male LS patients. MSH2 mutation carriers also had a higher proportion of prostate cancer vs non-MSH2 (7.8% vs 0.9%, p=0.017). There was no association between MSH2 mutation and bladder cancer (p=0.125). We found no association between the occurrence of upper urothelial, bladder or prostate cancers and colorectal carcinomas (CRC).

Multivariate analysis showed both MSH2 mutation (OR 5.47, 95% CI 1.18-25.23, p=0.00) familial history (OR 32.08, 95% CI 7.27-141.66, p<0.001) were significantly associated with the occurrence of urothelial cancers.

Conclusion: Despite the controversy regarding urothelial tumours surveillance in patients with LS, our study confirmed family history and MSH2 mutation as independent risk factors for urothelial cancers and a significant number of cases was diagnosed through surveillance. Therefore, we recommend regular screening in these high-risk subgroups. It is important to stress that urothelial cancers may be the index tumour in LS families and, because of that, awareness of urologists is of particular value.

Prostate cancer prevalence also seemed to be higher in MSH2 mutation carriers but additional studies are necessary to support its screening.

Disclosure: Nothing to disclose

P0682

BE AWARE TO EARLY ONSET COLORECTAL CANCER - THE EXPERIENCE OF A PORTUGUESE REFERENCE CENTER

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Introduction: Colorectal cancer (CRC) is one of the most common malignancies in the world. Although the incidence and mortality associated with CRC has steadily decreased in individuals over the age of 50 over the last several decades, the incidence of CRC in those under the age of 50 has been rising.

Aims & Methods: This retrospective study was designed to identify characteristics and risk factors for CRC in younger population. Medical records of individuals who were newly diagnosed with CRC between January 2018 and December 2019 were reviewed. Their previous endoscopic findings, family history of colorectal cancer, diabetes, body mass index (BMI), cigarette smoking, alcohol consumption, cholecystectomy in the past and the need for surgery, chemotherapy or radiotherapy as treatment option were analyzed. Those with the diagnosis of CRC with 50 years or less were considered to have early onset CRC.

Results: During the study period, 491 patients were newly diagnosed with CRC. Among them, 49 (10%) patients had early onset CRC, with average age at diagnosis of 44,4 years, with similar incidence among men and women (51% vs 49%).

As expected, the vast majority (90,9%) of patients had never performed any type of colorectal cancer screening, however it is worth noting the presence of two interval cancers within patients under 50 years. The location in the left colon, included the rectum, tended to be more frequent in the study group (79,6% vs 75,7%).

Early onset CRC was more common in patients with family history of CRC (24,5% vs 12,8%; $p=0,01$). The presence of diabetes in the study group was less than within the group of patients over the 50 years old (2% vs 25,3%; $p<0,001$).

Still, they tend to be more frequently submitted to chemotherapy and/or radiotherapy (24,5% vs 21,8%), but the percentage of patients undergoing surgery is similar between the groups. Despite the short period of follow-up, the mortality rate is surprisingly similar between groups.

In a multivariable analysis, interval cancer was highly related with family history of CRC (OR, 2,1; 95% IC:1,02-4,34; $p=0,04$) and the absence of diabetes (OR, 0,06; 95% IC: 0,008 - 0,426; $p=0,005$).

Conclusion: The early onset CRC tend to occur more frequently in the left colon and is more common in patients with family history of CRC and without diabetes. Younger patients would be expected to survive longer, however in the study population the mortality rate is similar, which makes the increase in the incidence of colorectal cancer in young patients even more worrying. Our study back-up the idea that it is crucial to review the age at which screening should begin, urgently.

More studies are needed, preferably prospective and multicentric in order to determine the best initial screening approach (rectosigmoidoscopy vs colonoscopy) in this young population and what is the ideal age to start screening for colorectal cancer in the most individualized way.

Disclosure: Nothing to disclose

P0683

FIRST-YEAR ADHERENCE TO THE HUNGARIAN POPULATION-BASED COLORECTAL SCREENING PROGRAM AND POTENTIAL INFLUENCING DEMOGRAPHIC FACTORS

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Introduction: Participation in colorectal cancer (CRC) screening programs significantly vary with 36-71% fecal occult blood test (FOBT) uptake rates, and compliance with referral for colonoscopy ranging 64-92% in Europe.

Aims & Methods: This observational cohort study aimed to assess first-year adherence to Hungarian population-based CRC screening program (EFOP-1.8.1-VEKOP-15-2016-00001), and to determine influencing demographic factors. We retrospectively analyzed participation data of the Hungarian population-based CRC screening program as of 31st December 2019, prospectively collected in National Public Health Institute's registry. Demographic data were retrieved from Hungarian Central Statistical Office database. Associations were assessed by Pearson's correlation coefficient.

Results: Of 528,745 invited individuals (20% coverage of target population), 186,916 (35%) picked up and 156,491 returned the screening kit, resulting in 30% adherence to FOBT [range between counties: 26-37%]. 14,628 individuals (9.3%) had non-negative results. 66% [53-82%] of the 9,340 persons referred to colonoscopy by the time of data acquisition, 6,154 individuals underwent screening colonoscopy. Considering additional 770 persons with non-negative FOBT who underwent colonoscopy outside the screening program (e.g. private sector), total adherence to colonoscopy as a screening method was 74% [59-98%]. Female gender, higher educational status and average monthly wage, lower number of inhabitants per GP slightly, while higher GDP per capita moderately correlated with adherence to screening colonoscopy.

Conclusion: Adherence rates to Hungarian CRC screening program comply with other European countries. Uptake of screening kits is low, but once picked up, kits are likely to be returned. Socio-economic factors may influence adherence to screening colonoscopy.

Disclosure: Nothing to disclose

P0684

RNA m⁶A METHYLTRANSFERASE METTL3 FACILITATES COLORECTAL CANCER BY ACTIVATING m⁶A-GLUT1-MTORC1 AXIS AND IS A THERAPEUTIC TARGET

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Introduction: RNA N⁶-methyladenosine (m⁶A) modification has recently emerged as a new regulatory mechanism in cancer progression. We aimed to explore the role of m⁶A regulatory enzyme METTL3 in colorectal cancer (CRC) pathogenesis and its potential as a therapeutic target.

Aims & Methods: The expression and clinical implication of METTL3 were investigated in multiple human CRC cohorts (n=551). The underlying mechanisms of METTL3 in CRC were investigated by integrative m⁶A-se-

quencing, RNA-sequencing and ribosome profiling analyses. The efficacy of targeting METTL3 in CRC treatment was elucidated in CRC cell lines, patient-derived CRC organoids and *Mettl3* knockout mouse models.

Results: Using targeted CRISPR/Cas9 dropout screening, we identified METTL3 as the top essential m⁶A regulatory enzyme in CRC. METTL3 was overexpressed in 62.2% (79/127) and 88.0% (44/50) of primary CRC from two independent cohorts. High METTL3 expression predicted poor survival in CRC patients (n=374, $P < .01$). Functionally, silencing METTL3 suppressed tumorigenesis in CRC cells, human-derived primary CRC organoids and *Mettl3* knockout mouse models. We discovered the novel functional m⁶A methyltransferase domain of METTL3 in CRC cells by domain-focused CRISPR screen and mutagenesis assays. Mechanistically, METTL3 directly induced m⁶A-GLUT1-mTORC1 axis as identified by integrated m⁶A-sequencing, RNA-sequencing, Ribo-sequencing and functional validation. METTL3 induced GLUT1 translation in m⁶A-dependent manner, which subsequently promoted glucose uptake and lactate production, leading to the activation of mTORC1 signaling and CRC development. Furthermore, targeting METTL3 significantly improved the anti-CRC efficacy of mTORC1 inhibitors in CRC patient-derived organoids and METTL3 transgenic mouse models.

Conclusion: METTL3 promotes CRC by activating m⁶A-GLUT1-mTORC1 axis. METTL3 is a promising therapeutic target for the treatment of CRC.

Disclosure: Nothing to disclose

P0685

PROGNOSTIC VALUE OF DELETION AND SINGLE NUCLEOTIDE POLYMORPHISMS OF COMMON GLUTATHIONE-S TRANSFERASES IN COLORECTAL CANCER PATIENTS

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Introduction: Glutathione-S transferases (GSTs) are large family of xenobiotic-conjugation enzymes involved the metabolism of know risk factors for colorectal cancer (CRC) development as well as chemotherapeutics used for CRC treatment. GST polymorphisms lead to alteration or complete lack of enzyme activity, which may have an effect on CRC development as well as response to chemotherapeutics and disease progression.

Aims & Methods: Aim of this study was to investigate GST gene variants as prognostic factors in patients with CRC. We have followed 523 CRC patients with a median of 34.8 months. A total of 70 patients received treatment with oxaliplatin. Deletion polymorphism of GSTs M1 and T1 was investigated by polymerase chain reaction. Single nucleotide polymorphism of GST A1 and P1 was investigated by restriction fragment length polymorphism method. Kaplan-Meier curves and Cox proportional hazards regression were used for the investigation of associations between genotypes and overall survival.

Results: GSTM1 null genotype was inversely associated with survival in CRC patients treated with chemotherapy (hazard ratio: 1.81, 95% CI: 1.22-2.68, $p = 0.003$). Furthermore GSTP1 variant genotype was also inversely

associated with survival in CRC patients (hazard ratio: 1.53, 95% CI: 0.67-2.46, $p = 0.048$). Neither polymorphisms of GSTA1 genotype nor GSTT1 genotype were significantly associated with CRC survival.

Conclusion: This study supports hypothesis that GST polymorphisms may have an important role in the process of the CRC progression. Additionally GSTM1 null and GSTP1 variant genotype may be predictive markers of oxaliplatin treatment.

Disclosure: Nothing to disclose

P0686

PARADOXICAL EFFECT OF PROBIOTICS MIXTURE AGAINST CLOSTRIDIUM DIFFICILE GROWTH INHIBITION

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Introduction: *Clostridium difficile* is the main cause of gastrointestinal illness, ranging from mild to profuse diarrhea with abdominal pain, or more severe conditions such as pseudomembrane colitis, sepsis, and sometimes even death. Many studies have demonstrated that *Lactobacillus* and *Bifidobacterium* are associated with colonization resistance against *C.difficile* and multi-strain probiotics are known to be more effective than the single strain probiotics.

In this study, we investigated whether the combination of *Bifidobacterium* and *Lactobacillus* could suppress the growth of *C.difficile*.

Aims & Methods: Based on our previous studies, we selected 3 strain of lactic acid bacteria (LAB), namely, *Bifidobacterium breve*, *B. animalis ssp lactis*, *Lactobacillus johnsonii* isolated from human feces that was able to attenuate growth of *C.difficile*. To evaluate for inhibition of *C.difficile* growth, we used a co-culture method. In order to co-culture multi-strain with *C.difficile*, The pellet and cell-free supernatant were collected by centrifugation(4000 r/min for 30min), and the pellet were washed twice in PBS, then, inoculated to BHI medium with *C.difficile* at the same ratio. Also, cell-free supernatants were prepared to concentrating with 100 KDa filter (Amicon® Ultra-15 centrifugal filter unit, Millipore) and *C. difficile* were inoculated. Cultures incubated for 24 hours under anaerobic conditions at 37°C. Antimicrobial ability of multi-strain against *C. difficile* was determined to evaluate *C. difficile* growth.

Results: Interestingly, multi-strain both pellet and supernatant showed that no antibacterial effects on *C.difficile*. The growth of *C.difficile* was significantly suppressed by the single strain(data not shown), but when combined, the results showed that the more growth of *C.difficile* rather than control.

The growth of *C.difficile* was not affected by the presence of LAB multi-strain and suggesting that when used as such combination there may be microbiota-microbiota interaction between multi-strain.

Conclusion: These results showed that combination could not suppress growth *C.difficile*. The presence of a variety of probiotic genera within a mixture may reduce its effectiveness through mutual inhibition by the dif-

ferent species, possibly by production of antagonistic agents, or by competition for nutrients. Therefore, further study of probiotics combination for inhibition of *C.difficile* of growth is currently needed.

Disclosure: Nothing to disclose

P0687

TO BE, OR NOT BE: HAMLET (HUMAN ALPHA-LACTALBUMIN MADE LETHAL TO TUMOR CELLS) TUMORICIDAL ACTIVITY IN COLORECTAL CANCER CELL LINES WITH DIFFERENT MUTATION STATUS *IN VITRO*

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Introduction: HAMLET (Human Alpha-lactalbumin Made Lethal to Tumor cells) is a proteolipid complex of partially unfolded α -lactalbumin and several oleate residues. Its efficacy as a selective killer of tumor cells has been documented *in vitro* and *in vivo* in several animal models [1]. HAMLET interacts with multiple tumor cell compartments, affecting cell morphology, metabolism, proteasome function, chromatin structure and cell viability [2].

Colorectal cancer is one of the most frequent malignancies worldwide, being second in males and third in females for its frequency and ranking fourth and third for cancer-related deaths among males and females, respectively [3]. KRAS and BRAF are major oncogenic drivers of colorectal cancer (CRC) [4].

Aims & Methods: **Aim:** This study aimed to evaluate tumoricidal activity of the HAMLET complex on three different CRC cell lines (LoVo, WiDr, Caco-2) with different mutation status (KRAS, BRAF or wild type).

Methods: **Cells.** Three different colorectal cancer cell lines were used for experiments: WiDr (BRAF gene mutation (mt) and KRAS wild-type (wt)), LoVo (BRAF wt and KRAS mt), Caco-2 (KRAS, BRAF wt). Cells were cultured in DMEM (WiDr) or F-12K (LoVo, Caco-2) media supplemented with 10 % fetal bovine serum (FBS) and 1 % penicillin and streptomycin, and cultured at 37°C in 5 % CO₂ incubator.

HAMLET complex was prepared using controlled temperature (partial protein unfold) combined with mixing/shaking with oleic acid additive (acid incorporation in protein structure) [5].

Cytotoxicity of the complex was evaluated using MTT assay. In order to evaluate HAMLET effects on cells metabolic activity, cells were seeded onto 96-well microplates and incubated for 6 h with different concentrations of HAMLET. After 6 h the medium was changed, and the absorption was measured at wavelength 570/620 nm, after 24 h of incubation at the normal growing condition.

Viability. Clonogenic assay was used to determine the viability of the cells. Cells were seeded onto 24-well plates and treated for 6 h with different concentrations of HAMLET in growth media. Afterwards, cells were allowed to grow for about 9-10 days at 37°C with 5% CO₂. Colonies were fixed and stained with crystal violet solution.

Results: Measurements of the metabolic activity of the colorectal cancer cells with different KRAS and BRAF gene mutation or wild-type showed that HAMLET reduced cells activity in a dose-responsive manner. 20 μ M concentration of HAMLET is cytotoxic to LoVo (cell viability 14.5 %) and Caco-2 (35.6 %) cells while WiDr cells are more resistant to this cytotoxic effect (88.2 %). Meanwhile, oleic acid, which is one of the components of HAMLET, did not affect colorectal cancer cells.

Clonogenic assay of colorectal cancer cells revealed that at 20 μ M HAMLET is cytotoxic to LoVo (14.5%) and Caco-2 (6.5%) cells while WiDr cells were more resistant (33%).

Conclusion: The results suggest that HAMLET affects cell metabolism, this effect is severe and at the same time irreparable for cells, leading to cell death. The complex exhibits cytotoxicity in a dose-response manner against all cell lines. However, BRAF mutant cells seem to be more resistant to HAMLET in comparison to KRAS mutants and wild type cells. HAMLET has anticancer potency for CRC *in vitro*.

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P0688

MUTATIONAL ANALYSIS OF COLORECTAL ADENOMATOUS POLYPS IN CHILDHOOD CANCER SURVIVORS TREATED WITH RADIATION THERAPY USING TARGETED NEXT GENERATION SEQUENCING (NGS)

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Introduction: Childhood cancer survivors treated with radiation therapy (RT) are at an increased risk of premalignant and malignant lesions, including early invasive colorectal carcinoma (CRC). It is well-established that RT-associated CRC undergo a preinvasive adenomatous stage where they can be detected and managed by early colonoscopy. Molecular profiling of these polyps using targeted NGS is highly sensitive and specific and may aid in unraveling their molecular composition. We aim to molecularly characterize colorectal adenomatous polyps in young cancer survivors treated with RT using a targeted NGS panel, as well as correlate the genetic findings with their histomorphology.

Aims & Methods: We extracted DNA from 18 adenomatous polyps which we acquired from 17 patients who received RT for childhood cancers. The median age is 35 at colonoscopy. The panel comprises 146 hotspots in 30 genes including: BRAF, KRAS, TP53, PIK3CA, PTEN and CTNNB1 etc. Four of the polyps had histopathologic diagnoses of sessile serrated adenoma/polyp (SSA/P) (22.2%), while the remaining 14 polyps were either tubular adenomas (TA), tubulovillous adenomas or TA with submucosal invasion (77.7%). High-risk features were defined as: size of 10 mm or greater, three or more adenoma, tubulovillous or villous histology or adenoma with high-grade dysplasia.

Results: Five polyps elucidated hotspot mutations at cancer-associated genes (27.7%), while the remaining 13 polyps were negative for the mutations tested (72.3%). Of the 5 mutated polyps, 2 polyps harbored substi-

tution mutations in the KRAS gene at exon 2. The two polyps were non-serrated and showed high-risk histological features. Additionally, 2 other polyps showed substitution mutations in the BRAF V600E, with both polyps showing histological features of SSA/P. The last mutated polyp had a histological diagnosis of TA with submucosal invasion and elucidated a substitution mutation at the TP53 gene.

Conclusion: Our analysis demonstrates that RT-associated polyps harbor similar genetic changes to adenomas in the average-risk population. We postulate that RT-associated polyps follow the conventional 'adenoma-carcinoma sequence' or the alternative serrated pathway, making them amenable to detection and management by early colonoscopy. Furthermore, our panel failed to detect novel driving mutations in cancer-associated genes. More comprehensive molecular analysis of these polyps is required to understand their molecular composition and to aid in identifying actionable genetic alterations.

Disclosure: Nothing to disclose

P0689

DIFFERENTIAL EFFECTS OF ANTIBIOTICS ON COLON AND RECTAL CANCER RISK AFTER BASELINE COLONOSCOPY NEGATIVE FOR CANCER: A TERRITORY-WIDE STUDY OF 97,162 PATIENTS

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Introduction: Recent studies suggested that antibiotics may modulate colorectal cancer (CRC) risk due to gut dysbiosis.

Aims & Methods: We aimed to investigate the effects of different antibiotics on CRC development in older subjects. We conducted a retrospective cohort study based on a territory-wide healthcare database of 7.4 million population. All patients aged at least 60 years who had undergone colonoscopy between 2005 and 2013 with no CRC found were recruited. We excluded cases with inflammatory bowel disease, prior colectomy, prior CRC and CRC detected < 6 months of index colonoscopy. Exposure of interest was any antibiotic use within 5 years before colonoscopy (including penicillins, cephalosporins, macrolides, carbapenems, quinolones, tetracyclines, aminoglycosides, nitroimidazoles, glycopeptides, sulpha/trimethoprim, and others). Outcomes of interest were PCCRC-all (all post-colonoscopy CRC diagnosed >6 months after index colonoscopy), PCCRC-3y (between 6 and 36 months after index colonoscopy), and PCCRC>3y (>36 months after index colonoscopy). Covariates included patient's factors, history of colonic polyps/polypectomy, concurrent drug usage (aspirin, NSAIDs, COX-2 inhibitors and statins) and endoscopy center's performance (polypectomy rate and colonoscopy volume). The adjusted hazard ratio (aHR) of PCCRC was calculated by multivariable Cox proportional hazards model. Stratified analysis was performed according to cancer subsites (proximal [cecum to splenic flexure], distal and rectal cancer) and nature of antibiotics (anti-anaerobic vs anti-aerobic, broad- vs narrow-spectrum, and oral vs intravenous route).

Results: Of 97,162 eligible subjects, 58,704 (60.4%) had antibiotic use before index colonoscopy. There were 1,026 (1.0%) PCCRC-all cases (694 [67.6%] PCCRC-3y and 332 [32.4%] PCCRC>3y cases). Antibiotic use was associated with lower rectal cancer (aHR:0.64; 95% CI:0.54-0.76) but higher proximal cancer risk (aHR:1.62; 95% CI:1.14-2.30). There was no statistically significant association between antibiotic use and distal cancer (aHR:0.99; 95% CI:0.76-1.30). Stratified analysis showed similar results for

PCCRC-3y but non-significant results for PCCRC>3y. Penicillins were associated with lower PCCRC-all risk (aHR:0.83; 95% CI:0.72-0.95), while aminoglycosides were associated with higher risk (aHR:1.54; 95% CI:1.05-2.26). Anti-anaerobic (aHR:1.67; 95% CI:1.17-2.39), narrow-spectrum (aHR:2.06; 95% CI:1.01-4.21) and intravenous antibiotics (aHR:2.59; 95% CI:1.36-4.92) were associated with higher proximal cancer risk, while broad-spectrum (aHR:0.63; 95% CI:0.53-0.75) and oral antibiotics (aHR:0.65; 95% CI:0.54-0.78) were associated with lower rectal cancer risk.

Conclusion: The effects of antibiotics on CRC in older patients varied according to cancer subsite, classes of antibiotics and route of administration. Further studies are necessary to elucidate the potential role of different antibiotics and gut microbiota on CRC development.

Disclosure: Nothing to disclose

P0690

MOLECULAR CHARACTERISTICS OF DEPRESSED EARLY COLORECTAL CANCERS

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Introduction: The adenoma-carcinoma sequence is generally recognized as a main route of colorectal cancers (CRCs). The development of endoscopic devices enables the detection of depressed and flat colorectal lesions, and some of these lesions are regarded as "de novo" cancers. Especially, depressed cancers invade massively into submucosa even when the size of tumor is small, and possess the malignant potentials to metastasis.

Aims & Methods: The aim of this study is to clarify the molecular characteristics of depressed CRCs with integrated genomic analysis using next-generation sequencer. We extracted DNA and RNA from 19 submucosal-invasive depressed CRCs and 8 submucosal-invasive protruded CRCs, and conducted whole exome sequence (WES) and RNA sequence (RNA-seq). We compared the mutation and copy number profile, and the expression of RNA using Gene Set Enrichment Analysis (GSEA), which enable to analyze the comprehensive gene expression in multiple molecular pathways, between depressed CRCs and protruded CRCs.

Results: The results of WES showed that the rate of KRAS mutation was significantly lower in depressed CRCs (5.3%) than protruded CRCs (62.5%). The copy number analysis showed that the amplification in 20p, 13p, and 13q arms were more frequently observed depressed CRCs (87.5%, 37.5%, and 37.5%) than protruded CRCs. Gene Set Enrichment Analysis using RNA-seq data clarified that the gene expression related to Epithelial-Mesenchymal Transition (EMT) and angiogenesis pathway were higher in depressed CRCs than protruded CRCs.

Conclusion: Our integrated genomic analysis showed that KRAS wild type and high copy number amplifications lead the overexpression of EMT and angiogenesis related genes in depressed CRCs, and these molecular characteristics would result in the malignant characteristics of depressed CRCs.

Disclosure: Nothing to disclose

P0691

CELLULAR FREQUENCY ANALYSIS WITH PYCLONE OF EARLY COLORECTAL TUMORS OBTAINED BY ENDOSCOPIC MUCOSAL RESECTION (EMR) AND ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)

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Introduction: In recent years, SMG which are key drivers of CRC development have been gradually investigated. On the other hand, details of cellular frequency (the ratio of cells with specific mutation) is still unclear especially among early colorectal cancer (CRC) and colorectal adenoma (CRA).

Aims & Methods: Thus the aim of this study was to investigate cellular frequency of early colorectal tumor obtained from EMR and ESD. By next generation sequencer, we analyzed nucleotides sequences of our endoscopically obtained CRA (8 patients, 6 EMR and 6 ESD) and 29 CRC samples (27 patients, 5 EMR and 24 ESD) by "Colorectal Cancer Panel" which we created In House. This In House panel covers 202,842 nucleotides or 67,614 deduced amino acids of 60 SMGs. Then we investigated cellular frequency of somatic mutation from allele frequency and copy number with PyClone analysis (<https://github.com/aroht85/pyclone>). In addition, we analyzed cluster of each mutation for multiple lesions within the same patient with PyClone analysis.

Results: Somatic mutation of Wnt signaling pathway (APC/RNF43/CTNNB1/AXIN2)/MAPK signaling pathway (KRAS/NRAS/BRAF)/Cell cycle signaling pathway (TP53/ATM/RB1) were 9 (75%)/ 5(42%)/0 (0%) in CRA and 21 (72%)/13 (45%)/18 (62%) in CRC. In both CRA and CRC, mutational gene of Wnt signaling pathway had high cellular frequency in each tumor especially with regard to RNF43. There were 6 patients with multiple lesions. In one patient with 2 different CRC, common somatic mutation of APC (Ser1144fs) was identified.

Conclusion: The cellular frequency with oncogenic mutation for Wnt signaling pathway were high in both CRA and CRC. Also, multiple lesions in the same patient could have common cluster. These characteristics might be crucial to understand tumor genomic characteristics of colorectal tumor.

Disclosure: Nothing to disclose

P0692

FREE FATTY ACID RECEPTOR DEPENDENT PRO- AND ANTI-TUMOR EFFECT OF SHORT CHAIN FATTY ACIDS (SCFAS) IN COLORECTAL CANCER - AN IN VITRO STUDY

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Introduction: Colorectal cancer (CRC) is the third most commonly diagnosed cancer in the world. Recent studies suggest involvement of free fatty acids (FFAs) and FFA receptors (FFARs) in the pathophysiology of CRC. FFARs consist of 4 types: FFAR2 and FFAR3 are activated by short chain fatty acids (SCFAs), while FFAR1 and FFAR4 are activated by long chain fatty acids (LCFAs). An increase in FFAR4 expression and decrease in FFAR2 expression are observed in patients with CRC. Moreover, there is evidence that FFAR4 ligands contribute to the development and progression of CRC

by affecting the migration and metastasis of cancer cells. On the other hand, SCFAs like butyrate and propionate are considered as anti-tumor agents, which induce growth arrest and apoptosis of CRC cells.

Aims & Methods: The objective of the study was to evaluate the effect of a synthetic FFAR2 agonist, 4-CMTB and FFAR4 agonist, GSK 127647 as well as combinations of natural SCFAs (acetate, butyrate at the concentrations of 50 and 2.5 mM, respectively) and LCFAs (stearate, palmitate, at the concentrations of 50 μ M) on cell viability in human colonic epithelial (CCD-841 CoN) and adenocarcinoma (HT-29) cell lines. Cell viability was determined after 48h incubation with tested compounds using MTT assay. qPCR was applied to identify the alterations in FFAR2 and FFAR4 expression.

Results: Synthetic FFAR2 agonist, 4-CMTB more significantly affected cell viability of HT-29 as compared to CCD-841 CoN at each tested concentration. In contrast, FFAR4 agonist, GSK 127647 was more cytotoxic to CCD-841 CoN cells as compared to HT-29 cells.

The combination of SCFAs as well as SCFAs in combination with LCFAs significantly reduced HT-29 cell viability ($p < 0.001$). Moreover, these combinations increased the expression of FFAR2 in HT-29 cell line ($p < 0.05$) as compared to control. Noteworthy, the combination of SCFAs as well as SCFAs with LCFAs significantly increased FFAR4 expression in CCD-841 CoN cell line as compared to control (untreated cells) ($p < 0.05$). In addition, the combination of SCFAs, but not SCFAs with LCFAs significantly elevated the expression of FFAR4 in CCD-841 CoN cell line as compared to HT-29 ($p < 0.05$).

Conclusion: This study confirmed anti-tumor properties of FFAR2 ligands: natural as well as synthetic FFAR2 agonists significantly decreased adenocarcinoma cell viability. Noteworthy, the anti-tumor effect of SCFAs was associated with elevated expression of FFAR2. Moreover, we observed that LCFAs do not modulate the anti-tumor properties of SCFAs. Surprisingly, the combination of SCFAs as well as SCFAs with LCFAs significantly increased FFAR4 expression in human colonic epithelial cells suggesting that FFAs may facilitate tumor growth. This is the first finding which suggests that SCFAs may cause opposite effect on CRC course, which is FFAR-dependent. Further experiments are pending.

Disclosure: Nothing to disclose

P0693

CLINICAL PROGNOSIS OF AKT 2 AND COX2 MUTATION IN ADVANCED COLORECTAL CANCER

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Introduction: Cancer has become one of the most mortal diseases in the world. The colorectal cancer (CRC) is the third more common type of cancer in men and the second in women around the world.

Studies have been improving the knowledge about the hallmarks of cancer, and that also includes CRC hallmarks. This similarity between the diseases shows predictors of evolution and therapeutic responses.

Recent studies have shown the impact of inflammation in CRC, this process is a possible key to understand the role pathogenesis process of CRC. This is a changing factor in cancer staging and prognosis knowledge. Carcinogenesis involves several been AKT2 and COX 2 pathways two of those. The AKT2 is a frequent alteration in CRC, it is a survival oncoprotein that regulates multiples cellular processes like growth, metabolism, proliferation and migration. In tumor cells the abnormal expression of the AKT2

can result from some major events like the overexpression or amplification AKT, over expression of his receptor, mutation or deletion of the suppressor gene PTEN or a negative regulator of PI3K.

The COX 2 is knowing as one of the keys to the colon carcinogenesis, is considered involved in inflammation and progression of different types of carcinomas. It is an inducible isoform that mediates prostaglandin synthesis during inflammation, an immediate-early response gene normally absent from most cells.

This article analyses the correlation between CRC and the inflammatory hallmarks AKT2 and COX 2.

Aims & Methods: The study used clinical and pathology database of 211 patients with advanced colorectal tumors from a private clinic in Ponta Grossa - Paraná - Brazil, who were submitted to surgery for the treatment of colorectal cancer from 2010 to 2015.

It was collected information from the medical records and prepared and analyzed the surgical blocks using hematoxylin-eosin (HE) technique, and organized in an arrangement of tissue microarray (TMA). The TMA preparation were prepared for immunohistochemistry for the following antibodies rabbit anti-COX-2 polyclonal antibody, 1: 200 and antibody rabbit polyclonal anti-AKT-2.

The slides were analyzed for marker expression, and then the markers expression, tumor staging and patient outcomes were analyzed to identify relationship between the markers and disease prognosis. Values of $p < 0.05$ indicated statistical significance.

Results: A total of 211 patients were analyzed with median age 63,4 ($\pm 13,0$), 110 (52,1%) female, 101 (49,1%) male. 72 (63,2%) were declared smokers in the medical record, 32 (30,8%) were declared alcoholics. 136 (66,7%) of the tumor was localized in the left colon, 48 (23,5%) were in the right colon and 20 (9,8%) in the rectal. 78,8% of the patients had partial colectomy. The COX2 sup was found in 200 patients, COX2 prof in 176, AKT2 sup in 199 and AKT2 prof in 192 patients.

About the metastasis, 60 (31,9%) of the patients had metastasis, was found no statistical relevance between the markers and metastasis.

For the marker COX2 sup was found a significant difference in the topographies, on the comparison the p result was 0,015 to right and left.

The presence of the AKT2 prof in the sample are correlated to decrease the survival time.

Was found a correlation between the presence of of the hallmarks, been only the akt2 prof and Cox2 sup not correlated.

Conclusion: In conclusion we found that in advanced CRC the presence of AKT2 deeply on the tumor brings a worse diagnosis. In long term the correlation between the mutations is lost as well as their harmful action decreases in significance.

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Disclosure: Nothing to disclose

P0694

BLOCKADE OF FRUCTOSE TRANSPORTER PROTEIN GLUT5 INHIBITS PROLIFERATION OF COLON CANCER CELLS - PROOF OF CONCEPT FOR A NEW CLASS OF ANTI-TUMOR THERAPEUTICS

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Introduction: Colorectal cancer (CRC) is the third most common diagnosed cancer in men (746 000 new cases per year) and the second in women (614 000 new cases per year). Although the improvements in detection and treatment decrease the incidence and death rate, CRC is still a great threat to human health. Diet is the most important risk factor apart from age, male sex and hereditary factors. Consumption of sugars is increasing worldwide; its association with cancer is still unknown. It has been suggested that high sugar diet may promote carcinogenesis by stimulation of insulin and insulin-like growth factor-I synthesis, induction of oxidative stress or promotion of weight gain. About 10% of the calories contained in the Western diet are supplied by fructose (approximately 55 g/day). Fructose is absorbed from the gastrointestinal tract through the passive transport across cell membranes by members of the glucose transporter family - GLUT. GLUT5 (class II) and GLUT2 (class I) are the major fructose transporters in the body. While GLUT2 is less selective, GLUT5 is the sole transporter specific for fructose with no ability to transport glucose or galactose.

Aims & Methods: The aim of the study was to assess whether GLUT5 inhibitor, N-[4-(methylsulfonyl)-2- nitrophenyl]-1,3-benzodioxol-5-amine (MSNBA), might decrease proliferation and viability of colon cancer cells.

Material and methods: In order to determine sensitivity of colon cancer cells to GLUT5 inhibitor, HT29 cells (colorectal adenocarcinoma) were exposed to different combinations of 1-1500 μ M MSNBA and 5-10 mM fructose for 24 and 48 h. Cell viability was assessed using the MTT test. Normal cell line CoN (colon epithelial cells) were used to provide cytotoxicity data.

Results: HT29 cells displayed 51% viability after 10 μ M MSNBA and 55% viability after 1 μ M MSNBA exposure for 24h. Additional presence of 10 mM fructose with MSNBA in the same concentrations did not statistically affect cell viability (respectively, 52 and 54%). After 48h treatment, cell viability remained similar (50% viability - 10 μ M MSNBA; 53% viability - 1 μ M MSNBA). CoN cells displayed 91% viability after 10 μ M MSNBA and 97% viability after 1 μ M MSNBA exposure for 42h.

Conclusion: This results suggest that GLUT5 expression in CRC can be indicative of the metabolic requirements and vascular supply of a tumor with clinical implications on patient survival and planning a course of therapy. GLUT5 expression may also be involved in evaluating tumor response to treatments and evaluation of residual disease.

Disclosure: Nothing to disclose

P0695 WITHDRAWN

P0696

NOVEL METHOD TO DETERMINE THE DEPTH OF INVASION IN COLORECTAL NEOPLASMS WITH ENDOSCOPIC ULTRASOUND ELASTOGRAPHY USING A FORWARD-VIEWING RADIAL-ARRAY ECHOENDOSCOPE

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Introduction: With the increasing use of endoscopy for treating colorectal cancer, accurate diagnosis of the depth of invasion in colorectal neoplasms has become an important clinical issue.

Aims & Methods: Our study aimed to compare the diagnostic ability and clinical efficacy of endoscopic ultrasound elastography (EUS-EG) with those of magnifying chromoendoscopy (MCE) and EUS in diagnosing the depth of invasion in colorectal neoplasms.

Patients with superficial colorectal neoplasms evaluated by MCE, EUS, and EUS-EG were enrolled. The primary clinical endpoint was the diagnostic yield differentiating intramucosal and shallow submucosal cancers from deep submucosal and advanced colorectal neoplasms, using the elastic score of colorectal neoplasms (ES-CRN). In addition, validation of ES-CRN was performed using inter- and intra-observer agreement from two expert and two non-expert endoscopists. We examined the diagnostic yield of additional patients prospectively due to these results.

Results: Thirty-one patients (33 lesions) with colorectal neoplasms were enrolled. The diagnostic yields (sensitivity, specificity, positive predictive value, negative predictive value and accuracy) of deeply submucosal cancers or advanced colorectal neoplasms, respectively, were as follows: EUS-EG: 100% / 88.2% / 86.7% / 100% / 93.3%, MCE: 66.7% / 94.4% / 90.9% / 77.3% / 81.8% and EUS: 93.3% / 77.8% / 77.8% / 93.3% / 84.8%. Interobserver agreement for the ES-CRN was 0.70 / 0.80 and 0.45 / 0.40 for the first/second assessment, for the two expert endoscopists and two non-expert endoscopists.

Furthermore, we examined additional 44 patients (47 lesions) prospectively. The diagnostic yields of prospective study were as follows, respectively: EUS-EG: 76.9% / 84.8% / 66.7% / 90.3% / 82.6%, MCE: 78.5% / 90.6% / 78.6% / 90.6% / 87.0% and EUS: 85.7% / 63.6% / 50.0% / 91.3% / 70.2%.

Conclusion: The diagnostic yield was from equal to higher for EUS-EG than for MCE and EUS, with moderate inter and intra-observer agreement, even for non-expert endoscopists. Therefore, EUS-EG may be a useful modality to determine the depth of invasion in colorectal neoplasms.

Disclosure: Nothing to disclose

P0697

CLINICOPATHOLOGICAL STUDY OF SERRATED LESIONS OF THE COLORECTUM

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Introduction: Serrated lesions of the colorectum are the precursors of microsatellite unstable carcinomas. However, their clinical and pathologic features are still unclear and need further exploration.

Aims & Methods: The aims of this study was to clarify the clinicopathological features of colorectal serrated lesions. We reviewed clinical charts and pathology files of 8312 endoscopically resected specimens performed during January 2007 and December 2019 in our hospital. A total of 806 serrated lesions (9.7%) resected were classified into three categories: HP (hyperplastic polyp), SSA/P (sessile serrated adenomas/ polyps), and TSA (traditional serrated adenoma), according to the WHO criteria. We examined the features of these cases and evaluate the morphologic characteristics by using immunochemical staining for Ki-67 and the expression of MUCs (MUC2, MUC5AC and MUC6) in differentiating serrated lesions.

Results: Of these 806 lesions, a total of 412 (51.1%) were HP, 231 (28.7%) SSA/P, and 163 (20.2%) TSA. Male to female ratio (M/F) was 2.26 for HP, 0.96 for SSA/P, and 2.04 for TSA. Mean size of SSA/Ps (12.5mm) and TSAs (13.2mm) were significantly larger than that of HP (8.1mm) ($p < 0.005$, respectively). SSA/Ps were located predominantly in the proximal colon, whereas HP and TSA were mainly located in the sigmoid colon and rectum. 82% of SSA/Ps were flat in macroscopic appearance. SSA/Ps and HPs were whitish or almost the same as adjacent mucosa in color, whereas TSAs had a tendency to be reddish. Magnified colonoscopy showed Type II open pit pattern as characteristic of SSA/Ps, whereas pinecone-shaped pit pattern as that of TSAs. Incidences of concomitant carcinomas in HP, SSA/P, and TSA were 0% (0 out of 412), 3.5% (8 out of 231), and 3.1% (5 out of 163), respectively. Ki-67 positive cells in HP showed regular, symmetric distribution, and those in SSA/P did irregular asymmetrical pattern, whereas most of those cells in TSA distributed in the so-called ectopic crypts. Expression levels of MUC2, MUC5AC and MUC6 were significantly different between serrated lesions, SSA/Ps and HPs were positive for MUC5AC in comparison with TSAs.

Conclusion: Our studies showed the three types of serrated lesions have their own distinct features and could be helpful to distinguish between them. SSA/P and TSA are premalignant lesions of colorectum and we should detect these lesions and completely remove endoscopically.

Disclosure: Nothing to disclose

P0698

DEVELOPMENT AND INITIAL EVALUATION OF THE VALID-CLASSIFICATION FOR PREDICTION OF COLORECTAL POLYP HISTOLOGY - A MULTICENTER INTERNATIONAL TRIAL

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Introduction: The recently introduced VIST chromoendoscopy technique allows for detailed analysis of surface and vascular pattern morphology.

Aims & Methods: The aim of this study was to create a new and unique classification for differentiating colorectal polyps using the VIST technology and to assess its interobserver concordance. In addition, we aimed to evaluate the accuracy of the new classification for optical diagnosis and histology prediction of colon polyps.

A digital library containing 26 videos/still images from 26 histologically confirmed polyps with VIST was first evaluated by seven endoscopists

from five different countries in order to identify possible descriptors. In the second step, the descriptors were categorized using a modified Delphi methodology to propose the VALID-classification. In the third step, the seven endoscopists independently reviewed a new dataset comprising of 45 videos/still images, and provided for each a diagnosis based on the VALID-classification. The interobserver agreement of the VALID-classification's individual descriptor was then assessed, and its accuracy in predicting colorectal polyp histology was evaluated.

Results: Using a modified Delphi process, the endoscopists agreed on summarizing 8 descriptors into three main domains. Those include polyp surface pattern morphology (regular, yes/no; irregular, yes/no; ulcerated, yes/no), and pit pattern morphology (regular, yes/no; tubular appearance, yes/no; villous appearance, yes/no; tubulovillous appearance, yes/no, no pits visible yes/no). Interobserver reliability calculated in Gwet's AC1 for the polyp surface and pit pattern morphology were 0.78 (0.57,0.82, 95%CI, the same as below) and 0.56 (0.46,0.67) respectively. The accuracy of the classification in predicting diagnosis (Non-neoplasia, Adenoma and Cancer) was 0.90 (0.84, 0.94), while the one in predicting the histology type (Hyperplastic Polyp, Tubular Adenoma, Tubulovillous Adenoma, Villous Adenoma and Cancer) was 0.70 (0.63, 0.77).

Conclusion: The new VALID-classification was developed allowing for prediction of colorectal polyp histology using the newly introduced VIST-chromoendoscopy technique. A good concordance was shown among the observers and a rather high accuracy of the VALID-classification has also been demonstrated in the initial video/still-image evaluation. Further *in vivo* trials are required to validate this new classification in a clinical setting.

Disclosure: Nothing to disclose

P0699

LAMIN A/C IS A POTENTIAL BIOMARKER IN COLORECTAL ADENOCARCINOMA

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Introduction: Lamin A/C are intermediate V-type filaments forming protein network between the nuclear membrane and the chromatin. These proteins are evaluated as biomarker or therapeutic target in many cancer. In colorectal cancer, only two studies with apparently contradictory results have reported that lamin A/C could be a new biomarker (1,2).

Aims & Methods: The main objective was to determine whether the expression of lamin A/C and specifically lamin A was correlated with survival and/or recurrence in colonic adenocarcinomas.

Secondary objective were : To compare lamin A/C expression between primary adenocarcinomas and their metastasis, to evaluate the correlation between lamin A/C expression and cell proliferation, to evaluate an automated immunohistochemistry assessment using Calopix Software.

Two double-spot microarray tissue (TMA) was studied. The first one was composed of 131 MSS colonic adenocarcinomas collected between 2002 and 2007 and the second of 59 corresponding metastasis. Lamin A/C, specific lamin A and Ki67 (to evaluated proliferation) antibodies was used. Immunostaining assessment was performed using the Histo-Score ("H-score", a semiquantitative score) as described in previous studies(3), in digitalized slides. Calopix Software was used to evaluated an automated "H-score" with the "immuno-object" program, in the tumor epithelial compartment and was compare to visual H-Score.

Results: For lamin A, mean survival time was shorter in the "High lamin A expression" group than in the "Low lamin A" group, with 48 months survival *versus* 123 months respectively (log-Rank test 4.29; $p < 0.038$). Recurrence rate was higher in the "high lamin A/C expression" group than in the "low lamin A/C expression" group (33% vs 8%, $p < 0.001$). This rate was also significantly for lamin A expression (44% vs 7%). The recurrence free survival was 141 months in "low lamin A/C" expression group and 69 months for high lamin A/C expression (Log rank = 4,39 $p = 0,036$). For the "low lamin A" group the mean time to recurrence was 143 and 46 months for high lamin A (log rank 11.28, $p < 0.001$).

Lamin A/C and Lamin A expression was significant higher in the metastasis than in the primitive tumor (lamin A/C, $p = 0.002$ and lamin A, $p = 0.005$). Expression of lamin A/C was inversely correlate with proliferation (Ki67) with a Spearman's coefficient at $p = -0.418$, $p < 0.0001$. Automated H-score obtained using Calopix software was highly correlated with visual analysis (Spearman 0,895, $p < 0,0001$).

Conclusion: High expression of Lamin A is associated with worse overall survival and more recurrence in colorectal adenocarcinoma. Their expression is higher in metastasis and is inversely correlated with proliferation. In addition, software could be an interesting tool to assess immunostaining.

References: (1)Willis et al, PlosOne 2008. (2) Belt et al Eur J Cancer. 2011. (3)Hirsch FR et al. J Clin Oncol. 2003.

Disclosure: Nothing to disclose

P0700

PREDICTING THE PATTERNS OF RESPONSE TO NEOADJUVANT CHEMORADIATION THERAPY IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER

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Introduction: To consider organ-preserving approaches for rectal cancer, favourable pathological response is needed. Since response is diverse, the goal of this project is to identify genetic predisposing factors and immune tumour microenvironment markers that could predict tumour response to therapy.

Aims & Methods: A cohort composed of 15 patients with complete tumour regression (TRG 0) and 15 patients with poor-or-no regression (TRG 3/4) was collected. Materials were formalin-fixed-paraffin-embedded biopsies and post-chemoradiotherapy resections. Next-generation sequencing was performed using a targeted gene panel. Histological tumour patterns of regression were determined. Immunofluorescence-multiplex was performed for several immune markers, as well as LC3-II stain for autophagy.

Results: Biopsies of bad responders tended to have higher intra-tumoural autophagy values compared to good responders. In tumour resections with response, intra-tumoural autophagy was higher in cases with a fragmented pattern compared to shrinkage pattern (p -value = 0.03). No clear difference in mutation patterns were observed. Results of the multiplex immunofluorescence stain of lymphocytes associated with the tumour will follow.

Conclusion: We showed a biological correlation between autophagy and tumour response pattern. The beneficial pattern of shrinkage is associated with low intra-tumoural autophagy. In advanced cancer cases, autophagy is considered a tumour growth promoter and is associated with tumour fragmentation.

Disclosure: Nothing to disclose

P0701

VALIDATION OF COLORECTAL CANCER PREDICTION MODELS IN PRIMARY HEALTHCARE

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Introduction: Two fecal hemoglobin based prediction models, COLONPREDICT and FAST, for colorectal cancer (CRC) detection have been developed and validated in symptomatic patients performing colonoscopy. We need to validate them in primary healthcare before recommending its use in patients with symptoms associated with CRC.

Aims & Methods: The aim of this study is to evaluate the diagnostic performance of the prediction models for CRC detection in primary healthcare and to compare them with the fecal immunochemical test (FIT) alone. We designed a prospective diagnostic test study. Symptomatic patients attending primary healthcare were offered to participate in the study. Symptoms and demographic information were collected and a FIT and a blood analysis to determine hemoglobin and carcinoembryonic antigen were performed. Colonoscopy was requested directly from primary healthcare under the general practitioner criteria.

We evaluated the discriminatory ability of COLONPREDICT, FAST and FIT for CRC detection using the area under the curve (AUC) and the sensitivity and specificity at the pre-established thresholds. In patients that performed a colonoscopy, we also evaluated the diagnostic accuracy for CRC and significant bowel disease (SBD).

Results: Out of the 437 symptomatic patients that accepted to participate in the study, 337 patients performed the blood analysis and delivered the fecal sample and 116 performed a colonoscopy. A CRC was detected in 12 patients and a SBD in 41. No CRC was detected in the patients that did not perform a colonoscopy after 16.5±3.1 months.

The AUC for CRC detection of COLONPREDICT, FAST and FIT in the study cohort was 0.94 (95% CI 0.91-0.98), 0.94 (95% CI 0.90-0.98) and 0.94 (95% CI 0.90-0.97). The sensitivity for CRC was 100% in all thresholds except for COLONPREDICT 5.6 (91.7%). On the contrary, specificity ranged between 84.7% (COLONPREDICT 5.6) and 36.3% (FAST 2.12).

The specificity of FIT at the 10 and 20 µg/g feces thresholds was 77.5% and 82.2%, respectively. The discriminatory ability of COLONPREDICT, FAST and FIT for CRC detection in the patients that performed the colonoscopy was 0.88 (95% CI 0.80-0.96), 0.86 (95% CI 0.77-0.95) and 0.85 (95% CI 0.76-0.93), respectively. The diagnostic accuracy for SBD was 0.74

(95% CI 0.64-0.84), 0.72 (95% CI 0.62-0.82) and 0.73 (95% CI 0.63-0.82). The sensitivity and specificity at the different thresholds are shown in the attached table.

		COLONPREDICT		FAST		FIT	
		>5.6	>3.5	>4.5	>2.12	≥10µg/g	≥20µg/g
CRC	Sensitivity	91.7%	100%	100%	100%	100%	100%
CRC	Specificity	69.2%	35.6%	56.7%	26.9%	50%	54.8%
SBD	Sensitivity	63.4%	85.4%	73.2%	90.2%	82.9%	75.6%
SBD	Specificity	77.3%	41.3%	64.0%	32.0%	60.0%	62.7%

[Sensitivity and specificity at the different thresholds in patients that performed colonoscopy]

Conclusion: The fecal hemoglobin based prediction models do not improve the discriminatory ability of FIT for CRC detection in symptomatic patients attended in primary healthcare.

Disclosure: Nothing to disclose

P0702

DATA INTEGRATION OF STOOL MICROBIOTA, PROTEOME AND AMINO ACID PROFILES TO DISCRIMINATE PATIENTS WITH ADENOMAS AND COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) ranks third in cancer incidence and second in cancer mortality worldwide. Current population-based screening reduces mortality but has limited sensitivity for CRC and its precursor lesions.

Aims & Methods: In this study, we aimed to integrate fecal microbiota, amino acid profiles and human proteome to explore potential biomarker panels for CRC and adenoma detection. In addition, we sought to gain insight into the interaction of gut microbiota and human metabolism in the presence of these lesions.

This multicenter case-control cohort was performed between February 2016 and November 2019 in two district hospitals and one tertiary referral center in The Netherlands. Consecutive patients ≥ 18 years with a scheduled colonoscopy were asked to participate and divided into three subgroups: CRC, adenomas and controls. In total, 12 CRC were randomly matched on age, gender, body-mass index and smoking habits to 21 adenoma patients and 20 controls without endoscopic abnormalities. Participants collected fecal sample prior to bowel preparation on which proteome (LC-MS/MS), microbiota (16S rRNA profiling) and amino acid (HPLC) composition was assessed. Least Absolute Shrinkage and Selection Operator and Elastic Net were used for feature selection. Selected markers were combined to obtain best predictive biomarker panels. Pearson correlation-based analysis on selected features was performed to create networks of all omics platforms.

Results: We identified markers within proteomic, microbial and amino acid platforms. Maximum area under the curve (AUC) for individual markers were 0.95 for CRC versus controls (HBA1), 0.89 for adenoma versus controls (ethanolamine) and 0.86 for CRC versus adenoma (sulfo-L-cysteine). Integration of data sets revealed markers associated with increased blood excretion, stress- and inflammatory responses and pointed towards downregulation of epithelial integrity. Combination of omics platforms led to the selection of new biomarker panels which outperformed AUC of hemoglobin in this cohort, which is currently used in population based CRC screening (AUC 0.98, 0.95 and 0.87 for CRC vs controls, adenoma vs controls and CRC vs adenoma, respectively).

Conclusion: Integrating platforms of fecal microbiota, proteomic and amino acid data provides for new predictive biomarker panels that may improve non-invasive screening for adenomas and CRC, and may subsequently lead to lower incidence and mortality of colon cancer.

Disclosure: S Bosch has nothing to declare. A Acharjee has nothing to declare. I Bijnsdorp nothing to declare, Patricia Rojas has nothing to declare, A Bakkali has nothing to declare. EEW Jansen has nothing to declare. P Stokkers has nothing to declare. J Kuyvenhoven has served as a consultant for Janssen Pharmaceuticals. A Henneman has nothing to declare. C Jimenez has nothing to declare. EA Struys has nothing to declare. Georgios V Gkoutos has nothing to declare. TGJ de Meij has served as a speaker for Mead Johnson. He has received a (unrestricted) research grant from Danone and MLDS. NKH de Boer has served as a speaker for AbbVie and MSD. He has served as consultant and/or principal investigator for TEVA Pharma BV and Takeda. He has received a (unrestricted) research grant from Dr. Falk, TEVA Pharma BV, Takeda and MLDS.

P0703

ACCURATE DIAGNOSIS OF SESSILE SERRATED ADENOMA/POLYP BY MAGNIFYING NARROW-BAND IMAGING: A PROSPECTIVE CONTROLLED STUDY

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Introduction: Magnifying narrow-band imaging (M-NBI) has recently improved the accuracy of endoscopic diagnosis of gastrointestinal tumors, including colorectal polyps. However, it can be difficult to distinguish be-

tween sessile serrated adenoma/polyps (SSA/Ps) and other polyps, especially hyperplastic polyps (HPs), by histological biopsy because diagnostic features of SSA/P can be detected around the colonic crypt bases.

Aims & Methods: We aimed to evaluate the accuracy of endoscopic diagnosis of SSA/P using M-NBI and compared it with histological biopsy. We enrolled patients diagnosed with SSA/P by preoperative endoscopy and assessed diagnostic accuracy. The diagnostic criteria for SSA/P were those of NBI International Colorectal Endoscopic Classification Type 1, with expanded crypt openings and/or thick and branched vessels [1]. The lesions were endoscopically resected and biopsy specimens were removed from the center of the resected lesions. Histological diagnosis was made by a pathologist who was blind to the endoscopic and biopsy diagnoses. The primary outcome was the accuracy of endoscopic and biopsy diagnoses.

Results: Between August 2015 and October 2017, 293 lesions were resected by polypectomy or endoscopic mucosal resection (EMR), and 79 endoscopically resected specimens that were endoscopically diagnosed as SSA/P were examined histologically. Two lesions were excluded because their specimens were too small for histological examination. Finally, 77 endoscopically resected lesions (64 resected by EMR, 6 by cold polypectomy, 4 by polypectomy and 3 by underwater EMR) and 77 biopsy specimens were assessed histopathologically and included in the analysis. The median resected tumor size (range) was 12 (6-23) mm. Histopathological examination showed 67 SSA/Ps, 8 HPs and 2 adenomas.

Number of patients/polyps	64/77
Male/female	29/33
Age (years, Median)	68 (38-87)
Location (n): Cecum, Ascending colon, Transverse colon, Descending colon, Sigmoid colon, Rectum	12, 30, 18, 8, 6, 3
Polyp size (mm, Median)	12 (6-23)
Morphology (n): Is, Lsp, Ila	17, 2, 58
Resection method (n): EMR, Cold polypectomy, Polypectomy, Underwater EMR	64, 6, 4, 3
Pathological diagnosis of endoscopic resection (n): SSA/P, HP, Adenoma	67, 8, 2

[Baseline data]

The sensitivity, specificity and accuracy of endoscopic M-NBI diagnosis for SSA/P were 95.7%, 95.5% and 95.5%, respectively. The sensitivity, specificity and accuracy of histological diagnosis of a single biopsy specimen were 71.6%, 90.0% and 74.0%, respectively.

Conclusion: This study shows that M-NBI may be useful for endoscopic diagnosis for SSA/P in a daily clinical setting and there is a possibility that biopsy could be avoided in patients with suspected SSA/P by M-NBI.

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Disclosure: Nothing to disclose

P0704

THE PROGNOSTIC VALUE OF THE TUMOR-STROMA RATIO IN NON-PEDUNCULATED T1 COLORECTAL CANCER: A MULTICENTER CASE-COHORT STUDY

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Introduction: Current risk stratification models for early-invasive colorectal cancer (T1 CRC) are not able to accurately discriminate between prognostic favorable and unfavorable tumors, resulting in overtreatment of a large (>80%) proportion of T1 CRC patients. The tumor-stroma ratio (TSR), which is a measure for the relative amount of desmoplastic tumor stroma, is reported to be a strong independent prognostic factor in advanced stage CRC, with a high stromal content being associated with worse prognosis and survival. We aimed to investigate whether the TSR predicts clinical outcome in patients with non-pedunculated T1 CRC.

Aims & Methods: Hematoxylin and eosin (H&E) stained tumor tissue slides from a retrospective multicenter case-cohort of patients with non-pedunculated, surgically treated T1 CRC were assessed for TSR by two independent observers, blinded for clinical outcomes. The primary endpoint was adverse outcome, which was defined as the presence of lymph node metastasis (LNM) in the resection specimen and/or (local or distant) CRC recurrence during follow-up.

Results: All 261 patients of the case-cohort had H&E slides available for TSR scoring; 183 were scored as stroma-low and 78 as stroma-high. There was moderate inter-observer agreement ($\kappa = 0.42$). In total, 41 patients

had LNM, 17 patients had recurrent cancer, and 5 had both. Stroma-high tumors were not associated with an increased risk for an adverse outcome (adjusted hazard ratio: 0.66, 95%-CI 0.37-1.18; $p = 0.163$).

Conclusion: Our study further emphasizes that existing prognosticators may not be simply extrapolated to T1 CRCs, even though their prognostic value has been widely validated in more advanced stage tumors.

Disclosure: Nothing to disclose

P0705

EPIGENOME - WIDE DNA METHYLATION PROFILING OF NORMAL APPEARING MUCOSA REVEALS HLA-F HYPERMETHYLATION AS A POTENTIAL NOVEL BIOMARKER CANDIDATE FOR SERRATED POLYPOSIS SYNDROME

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Introduction: Serrated Polyposis Syndrome (SPS) is associated with a higher risk for colorectal cancer. Intense promoter hypermethylation is a frequent molecular finding in the serrated pathway of colorectal carcinogenesis and may be present already in normal mucosa predisposing to the formation of serrated lesions. However, thus far, the methylation profile has not yet been analyzed in normal mucosa of SPS patients in an epigenome-wide fashion and on a single nucleotide level.

Aims & Methods: Fresh frozen samples of normal mucosa of the proximal and distal colon from 50 patients with SPS and 16 healthy individuals were analyzed by using the 850K BeadChip Technology (Illumina). Gene expression analysis was performed on the same samples by using Affymetrix array and correlated to methylation status of the corresponding differentially methylated regions (DMR). For validation, the 850K BeadChip was used to analyze FFPE tissue of the normal mucosa from an independent cohort of 17 SPS patients and 10 healthy controls. As a second validation step, we analyzed the methylation profile of direct specimens of 24 serrated lesions (6 hyperplastic polyps and 18 sessile serrated lesions).

Results: In normal mucosa, the most frequently hypermethylated genes were *HLA-F*, *SLFN12*, *HLA-DMA* and *RARRES3*; and the most frequently hypomethylated genes were *PIWIL* and *ANK3* ($\Delta\beta=10\%$, $P<0.05$). In FFPE tissue of the independent cohort, we could positively validate *HLA-F*. Expression levels of *HLA-F*, *SLFN12* and *HLA-DMA* were significantly different between SPS patients and healthy individuals and correlated moderately with the methylation status of the corresponding DMR (fold change >20%, $|R^2|>0.55$, $P<0.001$). Significant hypermethylation of CpGs in the gene body of *HLA-F* was also found in direct tissue of serrated lesions ($\Delta\beta=23\%$, $FDR=0.01$).

Conclusion: Epigenome-wide methylation profiling has revealed numerous differentially methylated CpGs in SPS patients in promoter, intra and intergenic regions. Significant hypermethylation of the gene body of *HLA-F* in normal mucosa was associated with a significant decrease in its expression levels and was also found to be hypermethylated in direct serrated polyp tissue. Hence, *HLA-F* is a novel promising biomarker candidate for SPS.

Disclosure: F.B. declares that he has endoscopic equipment on loan from Fujifilm, and has received an honorarium for consultancy from Sysmex and speaker's fees from Norgine. The other authors declare no competing interests.

P0706

DEVELOPMENT OF A NON-INVASIVE TRANSCRIPTOMIC SIGNATURE FOR THE IDENTIFICATION OF LYMPH NODE METASTASIS IN T1 COLORECTAL CANCERS

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Introduction: Endoscopic resection is now widely accepted as a radical treatment for T1 colorectal cancers (CRC) at low risk of lymph node metastasis (LNM), whereas additional surgical resection including lymph node dissection is recommended for T1 CRCs at high risk for LNM, even if they are endoscopically resected with negative margin. The current risk stratification for LNM of T1 CRCs is based on the postendoscopic pathological evaluation including invasion depth, lymphovascular invasion and degree of differentiation and tumor budding. We previously showed that more than 70% of T1 CRCs are classified as high risk, while postsurgical pathology results indicate only 12% of high risk cases are truly lymph node metastasis positive. This result highlights the necessity of other robust modality to predict LNM to avoid unnecessary radical surgical treatments.

Aims & Methods: We recently reported tissue-based miRNA or mRNA signatures associated with LNM in T1 CRCs. The present study aimed to establish an optimal transcriptomic signature to predict LNM in T1 CRCs through integrated miRNA and mRNA analysis. More importantly, we translated this tissue-based signature into a blood-based, non-invasive assay, for an easier and facile serologic diagnosis of these lesions. 162 tissue samples of high risk T1 CRC patients were subjected to qRT-PCR analysis for previously identified miRNA and mRNA signatures. Logistic regression model was adopted to create an optical integrated transcriptomic signature associated with LNM. The diagnostic value of this signature was assessed by qRT-PCR analysis using 142 matched serum samples.

Results: Among 162 tissues from T1 CRCs, 16 (9.9%) were LNM positive. 4 miRNA signature (miR-181b, 193b, 195 and 411) and 5 mRNA signature (AMT, FOXA1, PIGR, MMP1 and MMP9) identified LNM positive T1CRC with AUC value of 0.79 and 0.72, respectively. Integrated miRNA and mRNA signature further improved the diagnostic ability of LNM with a corresponding AUC value of 0.82. In analysis of 142 matched serum samples including 12 (8.4%) LNM positive, integrated RNA signature detected LNM positive T1CRC with AUC valued of 0.82. This RNA signature re-classified 71% of high risk T1CRC as low risk with 2% LNM and 29% as high risk with 24% LNM.

Conclusion: Our newly transcriptomic signature for non-invasive, liquid biopsy-based identification of T1 CRC has the potential to avoid the unnecessary surgeries for the patients classified as high risk by conventional risk-classification criteria.

Disclosure: Nothing to disclose

P0707

CHARACTERIZATION OF THE TUMOR-HOST INTERFACE AS A PROGNOSTIC FACTOR THROUGH DEEP LEARNING SYSTEMS

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Introduction: Interpretation of the tumor-host interface can provide relevant prognostic information. Through H&E and IHC double staining in combination with deep learning, we set out to find a novel way of characterizing features of the invasive margin in colorectal carcinoma (CRC).

Aims & Methods: Formalin-fixed-paraffin-embedded human CRC tissue obtained from the Radboudumc (Nijmegen, Netherlands) was automatically H&E stained and digitized. A double staining procedure using anti-CD3 and pan-cytokeratin was conducted on the same slides and scanned, generating a 2nd whole slide image (WSI) per sample. WSIs were processed using a series of deep learning neural networks (automated lymphocyte detection, tissue classification, tumor budding detection).

Results: Our method was successfully implemented as the tumor budding and lymphocyte detection algorithms were able to automatically detect peritumoral budding in pan-cytokeratin and CD3+ lymphocytes respectively in the immuno-stained WSIs. The tissue classifier segmented the H&E-stained WSIs into 13 classifications. This technique allows us to combine the relevant data and link the density of peritumoral budding with immune infiltration, tumor cell ratio, mismatch repair (MMR) status and clinical outcome. Data correlations on a cohort of 150 colorectal cancer patients with varied MMR status will be presented at the meeting.

Conclusion: Automated classification of the invasive margin combining clinical outcome can lead to an improved understanding of patient prognosis. This unbiased and transferable method could improve diagnostic accuracy and broaden our understandings of tumor budding and other poor prognostic factors.

Disclosure: Nothing to disclose

P0708

PROSPECTIVE REAL-LIFE PREDICTION OF FINAL HISTOLOGY AND REAL-TIME OPTICAL DIAGNOSIS OF NEOPLASTIC AND NON-NEOPLASTIC POLYPS DURING COLONOSCOPY USING A NEW ARTIFICIAL INTELLIGENCE DECISION SUPPORT SYSTEM (POLYPBRAIN®)

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Introduction: Precise differentiation between non-neoplastic and neoplastic polyps with high/low-grade dysplasia is important to assist optimal endoscopic therapy. New artificial intelligence-based decision support systems (AI-DSS) can help to support resect&discard strategy.

Aims & Methods: Our aim was to prospectively evaluate the precision of our recently developed Polypbrain® software and to compare final histology and real-time optical diagnosis of subcentimetric polyps in our everyday colonoscopy practice.

Polybrain® is an AI-DSS using deep learning neural network trained on our anonymous electronic database from a total of 1800 histologically identified sub-centimetric colorectal polyps and 26000 HD, electronic chromo-endoscopic images (malignant, juvenile, inflammatory and sessile serrated polyps were excluded). For this on-going prospective study, in every consecutive patients with 5-10 mm polyp, HD images were captured and histological diagnosis prediction (probability of hyperplasia or adenoma, LGD/HGD) was done real-time with Polybrain® during colonoscopy. All polyps were removed and finally, results were compared to histological diagnosis.

Results: 16 HD-BLI polyp images (hyperplastic/adenoma: 4/12 (dysplasia LG/HG: 8/4) of 16 patients (male/female: 11/5, mean age: 58.98 years) were included into this preliminary analysis. Mean count of subimages from each polyps were 160.31 (5-452). Feasibility of the predicted diagnosis was 96.48% for all polyps (adenoma: 96.42%, hyperplasia: 95.65%). Confidence in categorizing adenomas according to dysplasia grade was 69.94% and 69.69% in LGD and HGD group. Concordance between predicted and final histological diagnosis for hyperplasia or adenoma was 93.75%.

Conclusion: Polybrain® could provide a highly accurate tool for real-time optical diagnosis of polyps and to predict HGD. AI-DSS could not only support resect&discard strategy but might improve efficacy of endoscopic therapy to reduce polyp recurrence.

Disclosure: Nothing to disclose

P0709

BLOOD SERUM AND ERYTHROCYTE LIPIDOMIC PROFILING REVEALED DIAGNOSTIC BIOMARKERS IN PATIENTS WITH EARLY STAGES OF CRC AND ADENOMATOUS POLYPS

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Introduction: Objective: A) To investigate if discriminant lipidomics could be used as a potential diagnostic tool for early stages of colorectal cancer (esCRC) and precancerous condition adenomatous polyps (AP). B) to create a list of fatty acids (FAs) in the erythrocyte membranes (Er) and in blood serum (BS), the levels of which can be used as biomarkers of esCRC and AP. C) To investigate the accuracy of machine learning methods and different FAs sets to classify esCRC and AP patients from healthy individuals.

Aims & Methods: A total of 65 CRC patients with disease stages 1 and 2, as well as 25 patients with adenomatous polyps, and 35 conditionally healthy persons were included. The analysis of the Er and BS fatty acids (FAs) composition has been carried out using a gas chromatography-mass spectrometry (GC/MS) system based on the Agilent 7000B Triple Quadrupole (USA). Measured sets of FAs and two machine learning methods (support vector machine and random forest) were used to classify esCRC and AP patients from healthy participants as well as esCRC patients from AP.

Results: We have determined the levels of >30 FAs and their ratios in BS and Er membranes for the proband groups. The statistical analysis has identified eleven Er membrane FAs and fifteen BS FAs, which has made

it possible to distinguish the patients with adenomatous polyps from healthy individuals. We have identified coinciding trends for 9 markers concerning BS and Er membranes: the levels of the saturated FAs, e.g., C12:0 (p=0.0004-0.02), C14:0 (p=0.008-0.01), C 15:0 (p< 0.001), and mono-unsaturated FAs like 7-C16:1 (p=0.000005-0.02). We have obtained excellent results using the levels of discrete FAs in erythrocyte membranes to differentiate patients with adenomatous polyps from healthy ones: as for C15:0 pentadecanoic FA (AUC 0.819), as for palmitoleic FA 7-C16:1 (AUC 0.883), as for linoleic FA C18:2 n-6 (AUC 0.779), n-6/ n-3 (AUC 0.794), as well as for proportions of the FAs reflecting the activity of the delta-9-desaturase: 7-C16:1/saturated FAs (AUC 0.894), C16:0/7-C16:1 (AUC 0.890). The values C16:1 n-9, C16:2n-6, C18:1;9t, C18:2n-6, C22:6n-3, omega-6/omega-3 have been significant in differentiating patients with polyps from healthy ones (p=0.00001-0.006, AUC 0.73-0.89).

The statistical analysis has detected seven FAs in BS and Er membranes which could be considered biomarkers of early CRC stages: C14:0, C15:0, C20:2n-6, C22:5n-3, C22:6n-3, the sum of omega-3 FA, C20:5n-3+ C22:6n-3 (p=0.00009-0.018). Increased levels of C20:4 n-6 (p=0.000039) and a reduced ratio of omega-6/omega-3 (p=0.0019) have been detected additionally in BS of CRC patients. In the Er membranes, the level of differentiating metabolites has been also as follows: C16:1 n-9 (p=0.012), C18:3n-3 (p=0.021), C20:3n-6 (p=0.0028), C20:5n-3 (p=0.037), C22:4n-6 (p=0.00047), and for saturated FAs / unsaturated FAs (p=0.019). The AUC-ROC curve analysis of the diagnostic "panel" consisting of a list of the FAs described above has shown AUC value equal to 0.96 (sensitivity value 0.89, specificity value 0.93) when distinguishing of esCRC patients from healthy individuals.

Conclusion: This study demonstrates that the esCRC can produce a different lipidomic profile from AP and control subjects based on BS and Er samples. Machine learning models trained for classification of esCRC and AP create biomarkers. These data can be used as biomarkers of AP and esCRC with high diagnostic accuracy, which is promising for screening and early diagnosis of diseases.

Disclosure: Nothing to disclose

P0710

PROGNOSIS ANALYSIS OF PATIENTS WITH DISTANT METASTASIS IN NEWLY DIAGNOSED COLORECTAL CANCER: A POPULATION-BASED STUDY

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Introduction: Colorectal cancer (CRC) is one of the most common cancer worldwide, and a quarter of CRC patients presented with distant metastatic disease at initial diagnosis. Those patients diagnosed with distant metastasis have poorer prognosis.

Aims & Methods: Aims: This study aimed to investigate the distant metastasis pattern from newly diagnosed CRC and also analyze the long-term results of these patients.

Methods: Primary CRC patients, who were initially diagnosed from 2010 to 2016 in the SEER database, were included to analyze. Overall Survival estimates were performed using the Kaplan-Meier method with the log-rank test. Furthermore, multivariable Cox regression was obtained to identify covariates associated with increased all-cause mortality (ACM). Afterwards, colorectal cancer-specific mortality (CSM) was assessed by using Fine and Gray's competing risk regression. All of statistical analyses were performed using R 3.5.0 software.

Results: In this study, 57835 CRC patients, including 47823 without distant metastases and 10012 (17.31%) with metastases were identified. After analyses, patients with synchronous metastases, especially for those with cranial disease, were the poor prognosis. Furthermore, older age, unmarried status, poor or undifferentiated grade, right colon site, larger tumor size, N2 stage, more metastatic sites and elevated CEA might lead to poorer prognosis (all $P < 0.01$). For cancer-specific mortality, histology was also supported to be an independent factors associated to a shorter survival time.

Conclusion: In this population-based analysis, the incidence and prognosis for patients with distant metastases at time of newly diagnosis were estimated. The findings could help clinicians to identify high-risk patients with distant metastasis and provide proper treatment.

Disclosure: Nothing to disclose.

P0711

HISTOLOGICAL FEATURES OF THE REGIONAL LYMPH NODE METASTASES DEFINE SPECIFIC PATTERNS WHICH PREDICT SURVIVAL IN COLORECTAL CANCER

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Introduction: Regional lymph node assessment exists as a routine practice in pathologists work during the pN staging. Histological features of metastases are not reported separately because of the heterogeneity of individual metastases as well as their microenvironment. The prognostic significance and well defined histological patterns of lymph node metastases has not been established.

Aims & Methods: The aim of the study was to evaluate histologic features of the regional lymph node metastases and to assess the relation of their combination to disease prognosis.

The study was performed on the retrospective surgical material from 62 patients (25 male, 37 female, 64,6±10,7 years old) with lymphogenous-metastatic CRC. The patients underwent the surgery from 2009 to 2011 and were operated by the same surgeon. In summary 386 regional metastases were examined.

We determined the presence and the type of necrosis, stroma type, tumor grade, presence of nuclear polarity and clearly visible nucleoli, active inflammation, mucinous component, tumor budding and cytoplasmic podias, type and pattern of growth in the lymph node, presence of desmoplasia and the size of metastasis. Cluster analysis was performed to assess the histological patterns of metastases. We used Kaplan-Meier curves with the log-rank test (p_{lr}) for survival analysis. The impact of the single features was calculated by uni- and multivariate Cox regression.

Results: Cluster analysis revealed four main histopathological patterns of the regional lymph nodes. Every group was characterized by the typical features of this cluster. Based on the constellation of these features the pathologist can determine the pattern of the metastasis from 1 to 4 (Table 1).

We defined the prevalent lymph node pattern for every patient. 1 and 4 predominant patterns were associated with the lower progression-free ($p_r=0,002$) and tumor-specific ($p_r=0,017$) survival. The Cox regression showed worse effectiveness: only presence of necrosis ($p = 0,046$) and higher tumor grade ($p = 0,002$) predicted worse progression-free survival and tumor-specific survival. Thus, histopathological features need to be evaluated in the combination and to be reflected in the histopathological report.

Cluster/ features	Necrosis	Pattern of replacement	Type of growth	Mucinous component	Nucleus polarity	G	Tumor budding (median)
Cluster 1	present (geographical)	total	expanding	absent	absent	low grade	8
Cluster 2	present (intraglandular)	partial	infiltrative	absent	present	low grade	3
Cluster 3	absent	partial or portal	infiltrative	absent	present	low grade	4
Cluster 4	absent	total	infiltrative	present	absent	high grade	15

[Histopathological features corresponding to every cluster of the regional lymph nodes]

Conclusion: We described four predominant histopathological patterns of the regional lymph node metastases in CRC patients. The evaluation and reflecting of described features in histopathological report can predict the patients' prognosis and gives the ground for more detailed analysis of each pattern in the future.

Disclosure: Nothing to disclose

P0712

A LIQUID BIOPSY APPROACH TO DEFINE MACROPHAGE DYNAMISM IN METASTATIC COLORECTAL CANCER PATIENTS

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Introduction: In colorectal cancer (CRC), the inflammatory microenvironment strongly impacts on patients' outcome and a key role in this context is played by tumor associated macrophages. CRC patients displaying a dominant M2-like macrophagic population in the tumor infiltrate are characterized by an increased metastatic diffusion and poor outcome¹. Recent findings have also highlighted that tumor associated macrophages can affect the efficacy of both chemotherapy and target therapies²⁻⁴. Notably, it was put forward the possibility to detect tumor-derived macrophages in the peripheral blood of cancer patients, indicating the value of circulating M2-like cells as tumor indicators of advanced disease^{5,6}. However, the M1/M2 dichotomy initially proposed is a simplified interpretation of the real fluctuating state of these cells⁷. The wide variability of the macrophage phenotypes has been extensively demonstrated, highlighting the difficulty to define complex profiles based on a limited number of genes⁸.

Aims & Methods: The aim of the present study was to evaluate circulating macrophages as a dynamic biomarker that could be prognostic and allow to identify the CRC patients who will most benefit from targeted first-line treatments (including FOLFOX/XELOX/FOLFIRI/FOLFOXIRI plus bevacizumab or cetuximab/ panitumumab). To evaluate the circulating M2-like macrophages dynamism in CRC patients, we outlined a new signature of genetic expression aimed to evaluating specific macrophage markers in association with other leukocytic and angiogenetic indicators. Among these molecules, we investigated the potential of the extracellular protein EMILIN2 as a prognostic tool⁹⁻¹². EMILIN2 is expressed by the monocyte/macrophage lineage¹³ and, interestingly, EMILIN2 mRNA is enriched in macrophages upon IL-4/IL-13-induced M2-like phenotype^{8,14}. For the present retrospective study, we selected a cohort of 48 metastatic CRC patients whose liquid biopsy was available at the Institute Biobank.

Results: Preliminary studies were conducted on a small subgroup of cancer patients and healthy donors. The qPCR analyses performed on these buffy coats showed a large variability for most of the biomarkers included in the gene panel and to have a statistical relevant evaluation a major number of samples will be required. Interestingly, despite the small number of samples processed, these analyses indicated that EMILIN2 expression in the buffy coats of cancer patients was significantly higher compared to that of healthy donors.

Conclusion: We propose a liquid-biopsy based approach to evaluate the characteristics of circulating inflammatory cells in CRC patients. The development of new biomarkers specific for circulating macrophage may represent a useful and promising tool to predict the outcome of CRC patients and the response to chemotherapy and immune checkpoint inhibitors.

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Disclosure: Nothing to disclose

P0713

ASCERTAINMENT OF COLORECTAL CANCER BY LIQUID BIOPSY ASSESSING TWIST1 MRNA LEVELS IN BLOOD

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Introduction: Epithelial-to-mesenchymal transitions (EMT) occurs as a mechanism of invasion in colorectal cancer (CRC), and increased mRNA levels of EMT-transcription factors (chiefly TWIST1) are detectable in the blood of CRC patients (Celesti G., *Gastroenterology*, 2014). However, it is unknown whether circulating EMT-TF mRNA levels might help in identifying CRC patients and subjects with precursor lesions.

Aims & Methods: To assess whether increased levels of EMT transcription factors (TF) mRNAs circulating in the blood of patients with neoplastic lesions of the colon could serve as diagnostic tools, exploitable by a liquid

biopsy. By quantitative real-time PCR, we assessed the levels (as normalized threshold cycles, ΔCt) of TWIST1, ZEB2, and CDH1 EMT-TF mRNAs in blood samples of an institutional, consecutive cohort encompassing 236 CRC patients, 85 patients with advanced adenomas [including 45 cases with high grade dysplasia (HGD) adenomas], 91 cases with diminutive adenomas, and 296 controls (including 91 cases with diminutive adenomas). Blood samples were obtained before surgery and colonoscopy evaluation. Statistical comparison among ΔCt was managed by rank-sum test, and diagnostic modeling by logistic regression. Methods are covered by patent EP n.13197367.9.

Results: Circulating TWIST1 mRNA levels were higher in patients harboring advanced neoplasia, with a fold-change of 4.4 times for CRC (median $\Delta Ct = 26.3$), 2.8 times for HGD adenomas (median $\Delta Ct = 27$; both $p < 0.0001$), 1.5 times in advanced adenomas without HGD (median $\Delta Ct = 27.8$, $p < 0.003$), and 1.3 in diminutive adenomas (median $\Delta Ct = 28.0$, $p = 0.07$) vs controls (median $\Delta Ct = 28.4$). An age adjusted, logistic model, including TWIST1 and CDH1 mRNA levels properly identified 208/236 (88%) CRC, 31/45 (69%) HGD, 16/40 (40%) advanced adenomas, meanwhile classifying as negative 240/297 controls (i.e., 81% specificity). Consistently, the area under the curve at receiver-operator curve analysis for advanced neoplasia was 0.89. Overall, EMT-TF mRNA levels identified 80% of all advanced neoplasia, and 19% of false positives, with a positive predicted value of 81.73% compared with a negative predicted value of 78.43%.

Conclusion: Our pilot translational study strongly supports the feasibility of CRC diagnosis by an innovative liquid biopsy, assessing EMT-TF mRNA levels. Validation in larger series of neoplastic colonic lesions and proper controls is warranted. The excellent sensitivity for CRC and HGD adenomas also supports its use in pandemic times, in which access to endoscopic resources will likely become restricted and prioritizing of patients may become an issue.

References: ClinicalTrials.gov ID: NCT04323813

Disclosure: Luigi Laghi is inventor in co-participation of the patent no. EP13197367.9 - December 16, 2013.

P0714

PROTON PUMP INHIBITORS AND FAECAL IMMUNOCHEMICAL TEST FOR THE DETECTION OF ADVANCED NEOPLASIA IN SYMPTOMATIC POPULATION

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Introduction: The identification of the factors that are likely to influence the accuracy of the faecal immunochemical test (FIT) is of great importance for the colorectal cancer (CRC) screening programmes and for the screening of symptomatic patients. A Spanish cohort study found that the proton pump inhibitors (PPI) therapy reduces the accuracy of FIT in detecting advanced neoplasia (AN) in symptomatic population.

Aims & Methods: The aim of this study is to determine if these results can be reproduced in an independent population and can therefore be generalised. This is a prospective single centre study at the University Hospital of Coventry Warwickshire over a period of 14 months. Individuals who were referred for a diagnostic colonoscopy, on symptomatic pathway, were approached and were given a FIT prior to their colonoscopy. Their medication details were reviewed in-depth.

Results: A total of 612 individuals were included in the study. The positivity threshold of FIT used was 10 µg Hb/g faeces and the main outcome was AN. AN was detected in 9% (55) of the patients. The accuracy of FIT for detecting AN in PPI users and non-PPI users were sensitivity 54% vs 81%, $P = 0.05$; specificity 91% vs 90%, $P = 0.74$; positive predictive value 29% vs 47%, $P = 0.13$; and negative predictive value 96% vs 98%, $P = 0.41$, respectively. The ROC curves for FIT for the detection of AN in PPI users and non-PPI users were 0.74 (CI 95% 0.58±0.91) and 0.92 (CI 95% 0.89±0.95) respectively.

Conclusion: PPI therapy impairs the performance of FIT for the detection of AN in symptomatic patients. Given the widespread use of these drugs in the general population, the negative impact on the CRC screening programs could be substantial.

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Disclosure: Nothing to disclose

P0715

SIMULTANEOUS TESTING OF FECAL HEMOGLOBIN AND CALPROTECTIN PREDICTS THE DETECTION OF SIGNIFICANT COLORECTAL DISEASE IN THE WORK-UP OF SYMPTOMATIC PRIMARY-CARE PATIENTS: THE ADVANTAGE STUDY

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Introduction: The diagnostic yield of colonoscopy in patients with gastrointestinal symptoms is low and represents a major burden in open-access endoscopy units. (1). Retrospective studies have suggested that fecal immunochemical testing (FIT) and calprotectin may detect Colorectal Cancer (CRC) and inflammatory bowel disease (IBD) in the work-up of symptomatic patients, respectively. However, the accuracy of these tests for detecting significant colorectal disease (SCD) in primary-care (PC) symptomatic patients is unknown. We hypothesized that the simultaneous quantification of fecal hemoglobin and calprotectin may predict SCD detection, allowing for the implementation of a predictive model to optimize colonoscopy referral.

Aims & Methods: The primary aim of this study was to investigate the usefulness of FIT and fecal calprotectin test to create a new PC algorithm for colonoscopy referral.

This is a prospective multicentre international and observational study of symptomatic patients referred to colonoscopy carried out in 10 open-access endoscopy units in Spain and Portugal. Patients were recruited between February 2019 and February 2020. Inclusion criteria were:

- a) patients referred for the first time to colonoscopy by their general practitioner;
- b) having rectal bleeding, bowel habit change of >6 weeks, iron deficiency anaemia or abdominal pain with constitutional syndrome.

All patients referred for primary care were interviewed by a nurse to verify the inclusion criteria and to sign the informed consent. Eligible patients collected one fecal sample and were scheduled for FIT and fecal calprotectin before colonoscopy.

The main endpoint was the detection of SCD defined as presence of advanced adenoma, adenocarcinoma, segmental diverticular inflammation, angiodysplasia, inflammatory bowel disease, sessile serrated adenoma, synchronous neoplastic lesions or traditional serrated adenoma. Considering a minimum AUC of 75% (null hypothesis), an AUC greater than or equal to 85% (alternative hypothesis), and a prevalence of CRC of 5%, it would be necessary to evaluate 1,617 patients to obtain a strength of 90% and alpha significance of 5%. A multivariate analysis was performed to construct the predictive model.

Results: We report preliminary data with 991 patients (mean age: 59.9 ±15.3). Patients were divided into two different groups based on the need for colonoscopy. The first group (Grade 1) included those cases in which the colonoscopy results were normal, presented non advanced adenoma or a pathology that can be diagnosed using other techniques.

The grade 2 patients were those who had SCD that urgently required a colonoscopy. FIT showed an AUC of 0.69 (0.65-0.73); with a cut-off value for SCD detection of 2.55 µg/g feces had a sensitivity and specificity of 0.61 and 0.74 respectively and the negative predictive value (NPV) was 0.87. The calprotectin test showed an AUC of 0.64 with a cut-off value of 86.65 µg/g feces had a sensitivity and specificity of 0.73 and 0.53 respectively and NPV of 0.88. At the multivariate analysis the variables 'age', 'calprotectin test result', 'FOBTi test result', and 'gender' were independently associated with SCD detection, allowing the creation of a predictive model for colonoscopy referral.

Conclusion: The current study will provide a new decision tree algorithm to optimize the work-up of primary-care patients with lower abdominal symptoms referred for colonoscopy.

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Disclosure: AL, EQ, and FB are advisors to sysmex Iberica. Spain

P0716

EXTERNAL VALIDATION OF A FAECAL IMMUNOCHEMICAL TEST BASED-RISK SCORE FOR ADVANCED NEOPLASIA IN A BRITISH SYMPTOMATIC POPULATION

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Introduction: It has been demonstrated that the quantitative faecal immunochemical test (FIT) could be an accurate method for prioritizing symptomatic patients for the rapid detection of cancer. A quantitative FIT-based strategy performs better compared to the current high-risk symptoms-based strategies in fast tracking the suspected cancer referrals. A score, which combines quantitative FIT, age and sex to estimate the risk of advanced neoplasia (AN) in a symptomatic population, could help a physician in their decision-making process and in the proper allocation of endoscopic resources.

Aims & Methods: The aim of this study is to assess the performance of such a score in an independent British symptomatic patient cohort. Symptomatic individuals referred for a diagnostic investigations at University Hospital Coventry & Warwickshire were included. Patients were given a FIT HM-JACKarc prior to their investigations. The main outcome was AN. The risk score was assigned, ranging 0-11 points, according to the presence or absence of risk factors: sex (female=0, male= 2 points), age (< 40 years = 0, 41-50 years = 1, 51-60 years = 2, 61-70 years = 3, >70 years = 4) and positivity of FIT (< 10 µg Hb/g faeces = 0, ≥ 10 µg Hb/g faeces = 5). 10 µg Hb/g faeces was considered as the positivity threshold for FIT.

Results: 612 individuals were included and 51% (310) of whom were women. The mean age of the study cohort was 68 years. [IQR 57-76]. AN was detected in 9% (55) of the patients. Figure 1 shows the observed probability (dotted line) and expected probability (continuous line) of AN, according to FIT based-risk score. The table 1 shows number of individuals with and without AN in each risk score category. The expected probability was calculated based on the equation, developed through a logistic regression model in the Spanish cohort. The observed probability is the prevalence of AN in our study sample.

Conclusion: A risk score, which combines quantitative FIT, age and sex can accurately estimate the risk of having AN in a symptomatic British population.

References: Rodríguez-Alonso L, Rodríguez-Moranta F, Ruiz-Cerulla A, et al. An urgent referral strategy for symptomatic patients with suspected colorectal cancer based on a quantitative immunochemical faecal occult blood test. *Dig Liver Dis.* 2015;47(9):797-804. doi:10.1016/j.dld.2015.05.004

Disclosure: Nothing to disclose

P0717

QUALITY INDICATORS AND RESULTS OF COLONOSCOPY EXAMINATIONS IN THE FIRST YEAR OF HUNGARIAN POPULATION-BASED COLORECTAL CANCER SCREENING PROGRAM - A NATIONWIDE COHORT STUDY

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Introduction: The Hungarian population-based colorectal cancer (CRC) screening program (EFOP-1.8.1-VEKOP-15-2016-00001) was launched in 2019 among asymptomatic individuals between the ages of 50 and 70 with average risk of CRC.

Aims & Methods: We aimed to retrospectively assess the quality indicators and results of screening colonoscopies performed during the first year of screening program.

Our non-interventional, observational cohort study retrospectively analyzed clinical records of screening colonoscopies which were prospectively collected in the registry of National Public Health Institute. The quality indicators and results of examinations was determined based on cecal intubation rate, polyp, adenoma and cancer detection rates, proportion of photo-documentation and sedation.

Results: Total of 6407 colonoscopies were performed during the first year of CRC screening program from which the distribution of first and second examination was 6318:88. Cecal intubation rate was 93.48% (range: 88.67-98.21%), from which 67.19% (range: 1.81-98.21%) of cases were confirmed by cecal image documentations. The causes of incomplete colonoscopies were inadequate bowel cleansing (N=93, 18.60%), anatomical reasons (N=131, 26.60%) and malignant colonic obstruction (N=53, 10.60%), and only in 38 cases (7.60%), the examination had discontinued due to patients intolerance. Total of 88 second examination was performed due to polypectomy after completing first examination. 65.88% (range: 1.31-96.99%) of participants received some kind of sedation. The result of colonoscopy was non-negative in 84.27% (range: 76.92-94.89%) of cases. At least one polyp was found in 64.13% (N=4109) of participants (average 2 polyps, range 2-50; median: 2) among which the largest polyp was located in left-sided colon in 74.88% of cases and the polyp size was higher than 1 cm in 39.16% of cases. Morphological features of polyps could not be assessed due to inappropriate colonoscopy reports in registry. At least one polypectomy has been reported in 3574 cases, from which polyps' histological examinations were occurred in 86.98% of cases (adenoma: N=2468, 69.05%; non-adenomatous lesion: N=343, 9.60%; no histological result reported: N=763, 21.35%). Based on this, adenoma detection rate was 38.80%. CRC was found in 6.82% of participants from which the most cancers were located in the sigmoid colon (N=170, 38.90%) and rectum (N=142, 32.49%). Substantial difference was observed in terms of colonoscopy quality indicators between counties.

Conclusion: Cecal intubation, polyp and adenoma detection rates of screening colonoscopies of Hungarian CRC screening program are satisfactory according to guideline of European Society of Gastrointestinal Endoscopy, however, the description of polyp morphology, usage of advanced imaging assessment, polyp retrieval rate and the image documentation are inappropriate yet. The differences between counties are substantially influenced by the quality of reporting of colonoscopic results.

Disclosure: Nothing to disclose

P0718

REPEATING FAECAL IMMUNOCHEMICAL TEST FOR HAEMOGLOBIN IS A USEFUL STRATEGY TO AVOID NORMAL COLONOSCOPIES IN COLORECTAL CANCER SCREENING

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Introduction: Around 40% of colonoscopies performed in colorectal cancer (CRC) screening programmes are normal. New strategies are needed to reduce non-pathologic endoscopies in this setting. Bleeding associated with colonic lesions is intermittent, therefore, the positivity of the quantitative faecal immunochemical test (FIT) can be variable in different samples. Repeating FIT could be a useful strategy to reduce unnecessary colonoscopies.

Aims & Methods: To explore whether in those patients with a first FIT with a low positive determination ($\leq 50 \mu\text{gHb/g}$), a negative second FIT ($\leq 20 \mu\text{gHb/g}$) is associated with a low probability of CRC or high risk adenoma (HRA). Consecutive patients referred for colonoscopy in the CRC screening program were included. Patients were asked to perform a second FIT prior to the colonoscopy using the same test as the first FIT. CRC and HRA are considered relevant pathology. HRA includes advanced adenoma (defined as an adenoma with size $\geq 10\text{mm}$, villous component or high-grade dysplasia) and presenting ≥ 3 adenomas. Finally, we analyzed positive and negative predictive values (PPV and NPV), sensitivity (Se), specificity (Sp) and area under the ROC curve (AUROC) of the second FIT.

Results: 289 patients were included. Median age was 58.4 (IQR 54-62) years; 172 (59.5%) were men. CRC or HRA were detected in 80 patients (27.7%), whereas non-advanced adenomas were detected in 71 (24.6%), and 38.1% had normal colonoscopies. In 196 patients (67.8%) the second FIT was negative. Considering those patients with a low positive first FIT ($\leq 50 \mu\text{gHb/g}$) (n=120), the second was negative in 94 patients (78.3%). The diagnostic performance of the second FIT is summarized in following table.

	Number of patients	Second FIT positive	Se	Sp	PPV	NPV
All patients included	n = 289	n = 93	52.5%	75.6%	45.1%	80.6%
Patients with a first FIT < 50 $\mu\text{gHb/g}$	n = 120	n = 26	45.8%	84.3%	42.3%	86.1%

[Diagnostic performance of second FIT.]

The AUROC for the diagnosis of CRC and HRA was 0.679, and in those with a first FIT $\leq 50 \mu\text{gHb/g}$ was 0.697. With a low positive first FIT ($\leq 50 \mu\text{gHb/g}$) and a negative second test, the probability of significant pathology (adjusted by sex and age) was 69% lower than in the other possible results in first FIT (high positive result, $> 50 \mu\text{gHb/g}$) and second FIT (positive result) (OR 0.31, 95% CI 0.16 - 0.61).

Conclusion: In our CRC screening cohort, nearly 80% of patients with a low positive ($\leq 50 \mu\text{gHb/g}$) first FIT had a negative second FIT. A second FIT performed in patients with a low positive first test ($\leq 50 \mu\text{gHb/g}$), is a useful strategy to reduce the need to perform colonoscopies with no significant lesions in CRC screening programmes with low endoscopy capacity.

Disclosure: Nothing to disclose

P0719

RECLASSIFICATION OF SERRATED POLYPS AND ITS CLINICOPATHOLOGICAL SIGNIFICANCE - A 10-YEAR RETROSPECTIVE HISTOPATHOLOGICAL STUDY

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Introduction: Over the last 2 decades, besides the well-known adenoma-carcinoma sequence an alternative molecular mechanism of "serrated neoplasia pathway" has been recognised, responsible for approximately 30% of colorectal carcinomas (CRCs). Serrated polyps (SPs), accounting for 35% of all detected colon polyps, are classified into 3 subgroups - hyperplastic polyp (HP, 83-96%), sessile serrated lesion (SSL, 3-11%) and traditional serrated adenoma (TSA, 1-7%). HP is benign and lacks premalignant potential; however, SSL and TSA are known precursors to carcinoma. Endoscopic detection and histopathological evaluation of SPs are challenging and SSLs are frequently misclassified and labeled as HPs.

Aims & Methods: The primary aim of this study was to analyze histopathological features described in 6 major histopathological classification studies for the diagnosis of SSLs and to use these criteria to examine the reclassification rate of HP to SSL.

Histopathological slides of colorectal serrated lesions diagnosed between 2008 and 2017 at the 1st Department of Pathology and Experimental Cancer Research, Semmelweis University were retrieved and from these SPs diagnosed in 2014 were re-analyzed and if necessary reclassified using all the criteria described in the 6 major histopathological classification studies by 2 independent examiners under the supervision of an expert GI pathologist. Adherence and interval to post-polypectomy surveillance guidelines and association with CRC were also evaluated.

Results: After histopathological reclassification 253 patients with 274 polyps were found, including 215 HPs (78.6%), 10 SSLs (3.6%) and 6 TSAs (2.2%), and from these 8 HPs were reclassified as SSLs (2.9%) leading to an increased prevalence of SSL (6.5%). 35 polyps (12.8%) could not be evaluated properly due to the inappropriate biopsy sampling (missing lamina muscularis mucosae). A wide range of histopathological features was noted varying from 100% prevalence of basal crypt dilation to 22% prevalence of crypt serration (Table).

Basal crypt dilation	100%
Horizontal growth of the bases	67%
Epithelial/stromal ratio of > 50%	67%
Crypt branching	44%
Basal crypt serration	22%

[Prevalences of SSL histopathological features during reclassification]

In contrast to not redefined SSLs (50% right-sided, median size 7 mm), only 25% of all redefined SSLs were right-sided, and these were also 2 mm smaller (median size 5 mm). 75% of patients with SSL $\geq 10\text{mm}$ did not undergo post-polypectomy colonoscopy up 3 years later. In addition, every third SSL was associated with CRC.

Conclusion: Based on our results, SSLs might be underdiagnosed in our cohort, partly due to interobserver variability in histopathological interpretation, although adequate reclassification can improve the prevalence. As 12.8% of SPs could not be evaluated due to missing lamina muscularis

mucosae, adequate size biopsy and complete resection of SPs is of paramount importance in the proper diagnosis of SPs. It seems to be clear that a universal diagnostic criteria based on prospective clinicopathological studies is needed to avoid the under-diagnosis that may result in inadequate surveillance and increased risk of CRC.

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Disclosure: Nothing to disclose

P0720

ADHERENCE TO FECAL IMMUNOCHEMICAL TESTS AND COLONOSCOPY IN FAMILIAL COLORECTAL CANCER SCREENING: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: Colonoscopy is the most widely used procedure for non-syndromic familial colorectal cancer (NSCRC) screening. However, its effectiveness is limited by poor adherence. Recent evidence suggests that screening with fecal immunochemical testing (FIT) is equivalent to colonoscopy for detecting advanced colorectal neoplasia (ACN: CRC, advanced adenoma or serrated polyp) in familial CRC¹.

Aims: 1) To investigate whether the adherence to annual FIT screening is superior to direct colonoscopy in first-degree relatives (FDR) at high-risk of NSCRC;

2) To compare the diagnostic yield for ACN between the two screening strategies.

Methods: This is a prospective multicenter controlled randomized trial conducted in Spain between March 2016 and September 2019. 463 index cases with NSCRC diagnosed under the age of 60 were interviewed to perform a genealogical tree and to sign the informed consent. FDR inclusion criteria were: to have 1 index case < 60 yr, 2 index cases of any age at diagnosis or a brother with NSCRC. The exclusion criteria were: previous screening, personal history of ACN, inherited CRC syndrome, digestive symptoms or severe comorbidity. FDR were randomized (1:1) before signing the informed consent to direct colonoscopy or annual FIT for 3 years, with a cutoff for colonoscopy of $\geq 10 \mu\text{g Hb/g feces}$. Invitation to screening

was made by personalized letter through the index case. Assuming an adherence of 0.50 for colonoscopy and 0.60 for FIT, with an alpha and beta risks of 0.05 and 0.10 respectively, it was needed to include 538 FDR per group. An intention-to-treat analysis was performed.

Results: 1965 FDR were evaluated, of which 1035 were excluded for different reasons. Finally, 930 FDR were included, which were randomized to direct colonoscopy (n = 465) or annual FIT (n = 465). An interim analysis was performed after the inclusion of 86.4% of the estimated sample. Adherence to the FIT group (at least one test performed) was 162/465 (34.8%) and to the colonoscopy group 147/465 (31.6%), OR 0.86: CI 95% 0.65 -1.13, $p = 0.29$. A positive FIT was found in 22/162 (13.5%) cases, of which 19 (86.3%) underwent colonoscopy. In the colonoscopy group, 22 (15%) ACN (21 advanced adenomas and 1 CRC) were detected, while in the FIT group 8 (5%) ACN (7 advanced adenomas and 1 CRC) were detected, $P < 0.01$.

Conclusion: In FDR at high-risk for NSCRC, annual FIT screening does not improve the adherence to colonoscopy screening, with fewer advanced neoplastic lesions being detected. These data suggest that new strategies should be sought to improve adherence to screening in this population.

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Disclosure: Enrique Quintero is advisor to Sysmex Iberia

P0721

COLONIC STENTING IN ACUTE MALIGNANT OBSTRUCTION IN A TERTIARY REFERRAL CENTRE IN SINGAPORE - AN AUDIT OF SAFETY AND EFFICACY

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Introduction: Colorectal cancer (CRC) has been consistently ranked among the top three causes of cancer-related deaths worldwide. Acute large bowel malignant obstruction is one of the emergent presentations of CRC. Placement of a self-expandable metal stent (SEMS) for relief of obstruction has gradually progressed from a therapeutic modality with palliative intent to a role of bridging towards elective curative surgery to decrease peri-operative complications of emergent surgery in these scenarios.

Aims & Methods: We aim to review the safety and efficacy of SEMS placement in our patient cohort and present their degree of success in technical and clinical outcomes, as well as the rates of recurrence following surgery post-SEMS placement.

This is an audit of data from a prospectively maintained database of patients undergoing colonic stenting in a tertiary referral centre in Singapore. Technical success was defined as successful deployment of the SEMS across the tumour following passage of a guidewire. Clinical success is defined as adequate expansion of the stent with relief of obstruction not requiring further surgical decompression. Rates of complications such as bowel perforation, stent migration or tumour overgrowth were studied. Time to surgery, type of surgery and rates of recurrence in our cohort were also recorded.

Results: 79 patients underwent emergent SEMS placement for acute large bowel obstruction secondary to CRC from September 2013 to February 2020. Mean age 68.8 years (± 13.8 years), male 43/79 (54%). Obstruction was predominantly proximal to splenic flexure: rectum (4/79, 5.1%), rectosigmoid (14/79, 17.7%), sigmoid (30/79, 38.0%), descending (23/79, 29.1%) and transverse colon (8/79, 10.1%). Mean length of CRC was 4.44cm. Tech-

nical success was 94.9% (75/79) and clinical success was 94.7% (71/75). Complications were perforation (4/79, 5.1%), stent migration (2, 2.5%) and tumour ingrowth (1/79, 1.3%).

52/79 (65.8%) of SEMS were inserted as bridge to surgery. Mean time to surgery was 21.6 days ($\pm$ 12.3 days). 42/52 (80.8%) of patients underwent minimally invasive surgery (robotic surgery 7/42, 16.7%; laparoscopic surgery 35/42, 83.3%) while 10/52 (19.2%) underwent open surgery. 34 patients had follow-up for more than 1-year post-treatment (median 34 months) and underwent a median of 1 colonoscopy during this time. Local recurrence and distant metastasis were observed in 4/34 (11.8%) and 2/34 (5.9%), respectively.

Conclusion: Bowel decompression with SEMS in acute malignant obstruction has a high technical and clinical success rate, enabling the majority of these patients to undergo minimally invasive surgery. The commonest complication is perforation. SEMS placement in our study did not seem to adversely affect oncologic outcomes as rates of recurrence are similar to that reported in other studies.

Disclosure: Nothing to disclose

P0722

PRIMARY ENDOSCOPIC RESECTION HAS LONG-TERM PROGNOSIS SIMILAR TO THAT OF SURGERY FOR T1 COLORECTAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: The optimal therapeutic approach for T1 colorectal cancer remains controversial. Herein, long-term outcomes of endoscopic resection (ER) were investigated and compared with those of primary or additional surgery.

Aims & Methods: A systematic review was conducted using the PubMed, Embase, and Cochrane databases. Primary outcomes were overall survival, disease-specific survival, and recurrence-free survival at 5 years. Secondary outcomes were local recurrence and distant metastasis. Hazard ratios (HR) were used to calculate time-to-event data.

Results: In total, 17 published studies with 19979 patients were included. Meta-analysis exhibited similar overall survival (79.6% vs. 82.1%, HR = 1.13, 95% CI = 0.99-1.30), recurrence-free survival (96.0% vs. 96.7%, HR = 1.28, 95% CI = 0.87-1.88), and disease-specific survival (94.8% vs. 96.5%, HR = 1.09, 95% CI = 0.67-1.78) in patients with primary ER and primary surgery. In addition, additional surgery and primary surgery were equally effective in terms of recurrence-free survival (HR 1.27, 95% CI 0.85-1.89). However, ER alone was associated with worse overall survival than primary or additional surgery. Sensitivity analysis revealed that the ER group had significantly fewer procedure-related adverse events (2.1% vs. 10.9%, $P < 0.001$) than the surgery group. Lymphovascular invasion and rectal cancer, but not depth of submucosal invasion, were the independent predictors of recurrence. High-risk histology features, especially lymphovascular invasion were predictors of lymph node metastasis.

Conclusion: First-line ER should be strongly considered for endoscopically resectable T1 colorectal cancers. In cases of non-curative resection, additional surgery may have comparable outcomes to primary surgery.

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Disclosure: Nothing to disclose

P0723

CLINICAL FEATURES AND GENOMIC CHARACTERIZATION OF POST-COLONOSCOPY COLORECTAL CANCER

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Introduction: Some CRCs, or post-colonoscopy CRCs (PCCRCs), are diagnosed months or years after negative colonoscopies. Although most PCCRCs are considered to be lesions that have been missed at previous colonoscopies, they may have unexplained biological features different from other CRCs. This study aimed to determine the clinicopathological, biological, and genomic characteristics of PCCRCs.

Aims & Methods: A total of 1,619 consecutive patients with 1,765 CRCs were recruited. After excluding patients with inflammatory bowel disease, familial polyposis syndrome, CRCs that developed from diminutive adenomatous polyps, and recurrent CRCs after endoscopic resection, 32 patients with 34 PCCRCs, whose colonoscopies were negative at 6-60 months before diagnosis, were enrolled. The lesions' clinicopathological features, mismatch repair proteins (MMRs), and genomic alterations were investigated.

Results: The PCCRC rates were 1.9% (34/1,765) overall, 2.2% (18/821) for intramucosal (Tis), 2.1% (8/377) for T1, and 1.4% (8/567) for T2 or more deeply invasive cancers. More men (79%) than women (21%) had PCCRCs. All of PCCRCs were resected by ER alone, additional surgery after ER, or initial surgery. The 3-year survival rates for the patients with Tis, T1, and T2 or more deeply invasive cancers were 92% (12/13), 75% (6/8), and 57% (4/7), respectively. Thirty-three tumors' MMRs were investigated, and 7 (21%) exhibited deficient MMRs (dMMRs), comprising 4 with T2 or more deeply invasive cancer and 3 whose lesions were in the proximal colon. dMMRs were present in 50% of the T2 or more deeply invasive cancers, 29% of the T1 cancers, and 6% of the Tis cancers. Twenty-three tumors' genomic mutations were investigated, and BRAF and KRAS mutations were present in 3 (13%) and 12 (52%) cases, respectively. Two patients with dMMRs and BRAF^{V600E} mutations had poor prognoses. PIK3CA had mutated

in 5 of 6 T2 or more deeply invasive cancers, of which, 4 were located in the proximal colon. None of the cases with Tis or T1 PCCRCs had *PIK3CA* mutations. Sixty-one percent (17/28) of the macroscopic type 0 lesions were superficial. All superficial Tis and T1 PCCRCs were detected < 24 months after the negative colonoscopies, and they were distributed throughout the colon and rectum. Less superficial lesions, including type 2/3 lesions and type 0 lesions with polypoid morphologies, were more likely to be located in the sigmoid colon. None of the superficial lesions exhibited dMMRs. Compared with PCCRCs exhibiting proficient MMRs, those exhibiting dMMRs tended to be located in the proximal colon, and detected later when they were more deeply invaded.

Conclusion: PCCRCs can be deeply invasive cancers with dMMRs and/or a *PIK3CA* mutation that have the potential to grow rapidly and are associated with poor prognoses, and are located in the proximal colon, or missed early cancers that are either superficial lesions that can be located anywhere in the colon and rectum, or less superficial lesions in the sigmoid colon.

Disclosure: Nothing to disclose

P0724

COLORECTAL SURGERY IN PATIENTS WITH NONMALIGNANT LESIONS DETECTED IN A COLORECTAL CANCER SCREENING PROGRAM

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Introduction: Although colorectal cancer (CRC) screening programs reduce CRC incidence and mortality, they are associated with risks related to overdiagnosis and overtreatment.

Aims & Methods: The aim of this study is to describe the requirements of surgery in patients with nonmalignant lesions detected within the first round of a fecal immunochemical test (FIT) based CRC screening program. We included in this analysis all the patients that performed a colonoscopy after a positive FIT ($\geq 20 \mu\text{g}$ Hb/gr of feces) in the first round of the Galician CRC screening program between May 2013 and June 2019. We determined the surgery indication, the mean hospital stay, and the surgery associated mortality and morbidity rate. Patients were classified according to the most advanced lesion based on the European guidelines for quality assurance in CRC screening: normal, low, intermediate and high-risk adenomas and, finally, CRC. We calculated surgery rate according to the most advanced lesion, hospital, sex, age and fecal hemoglobin (Hb) concentration and we determined which variables were independently associated with surgery rate using a multivariable logistic regression analysis.

Results: In the analyzed period, 16,720 patients performed a work-up colonoscopy. The most advanced lesion was a CRC (6.1%), high (19.3%), intermediate (25.1%) and low risk (21.7%) adenomas and, finally, normal colonoscopy (27.8%). A colorectal surgery was performed in 158 (10.0%) out of the 15,707 patients included in the analysis due to endoscopic complications (0.2%) and treatment of benign lesions (9.7%). The mean hospital stay was 8.4 ± 10.1 days with 17.1% (27) patients developing minor

complications, 6.9% (11) major complications and death in 0.6% (1). After discharge, complications developed in 18.4% (29) patients. In patients with benign lesions, the mean size was 38.2 ± 19.3 mm, with Paris classification morphology II in 72 (46.7%). An endoscopic resection attempt was performed in 39 (25.3%) patients. In the surgical specimen, a premalignant lesion was detected in 89.7% (adenoma 127, serrated lesion 13). The rate of surgery was associated with the European guidelines risk classification (normal=0.8%, low=1.1%, intermediate=3.8% and high-risk adenoma=41.2%; $p < 0.001$), hospital (ranging between 2.7% and 12.7%; $p < 0.001$), sex (female=10.4%, male=9.6%; $p = 0.6$), age (<60 years=6.5%; ≥ 60 years=19.1%; $p < 0.001$) and fecal hemoglobin concentration (<100 μg Hb/g=7.3%, 100-200 μg Hb/g=13.4%, >200 μg Hb/g=17.6%; $p < 0.001$). In the logistic regression analysis, European guidelines risk classification (low risk OR 1.4, 95% CI 0.3-5.5; intermediate risk OR 5.1, 95% CI 1.7-15.4; high risk adenoma OR 61.4; 95% CI 22.5-167), sex (male OR 0.5, 95% CI 0.3-0.6) and age (≥ 60 years OR 1.5; 95% CI 1.1-2.2) were independently associated with the risk of surgery.

Conclusion: In a CRC screening program, the surgery rate in patients with nonmalignant lesions is low and mainly related to the characteristics of the detected adenomas.

Disclosure: Nothing to disclose

P0725

GREEN TEA EXTRACT TO PREVENT COLORECTAL ADENOMAS IN A COLORECTAL CANCER SCREENING POPULATION - FINAL RESULTS OF THE MIRACLE TRIAL

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Introduction: Epidemiological and experimental data suggest that green tea and in particular its ingredient epigallocatechingallate (EGCG) has an antineoplastic effect in the colorectum.

Aims & Methods: MIRACLE is a randomized, placebo-controlled, double-blind trial of decaffeinated green tea extract (GTE) standardized to contain 150 mg of EGCG to prevent colorectal adenomas. 1001 participants (age: 50-80 years) with histologically documented adenomas within the past 6 months were included in a 4-week run-in with GTE bid to assess its

safety. 879 participants were subsequently randomized to receive bid GTE (n=432) or placebo (n=447). Follow-up colonoscopy was to be performed 3 years after the qualifying endoscopy. Primary endpoint was the presence of one or more adenomas or colorectal cancer at the follow up colonoscopy.

Results: Groups were well balanced with respect to baseline characteristics. Green tea extract safety profile was favourable with no major differences in AEs. Adenoma rate in the mITT-set (n=632) was 55.7% in the placebo and 51.1% in the green extract group. This 4.6% difference was not statistically significant (one-sided 95%-CI: 1.018, p=0.081). A pre-planned analysis according to gender revealed an adenoma rate of 47.9% and 47.6% in the female placebo and green tea extract group, respectively (95%-CI: 0.771, 1.347; p=0.894). In male participants adenoma rate was 60.4% in the placebo and 52.9% in the green tea extract group (95%-CI 0.717, 0.999; p=0.048). Green tea extract intake was associated with a significant, 12.4% relative and 7.5% absolute reduction of metachronous adenomas in males.

Additionally, in the male subgroup was no difference between the placebo (10.8%) and the green tea extract group (11.3%) with respect to advanced adenomas (95%CI 0.609,1.848; p=0.835), but low-grade CA were significantly reduced in the male green tea extract subgroup: 34.4% vs. 43.8% in the male placebo group (95%CI 0.587,0.964; p=0.025). In the female population there were no differences. Thus, green tea extract intake significantly reduces recurrence of low grade, but not of advanced adenomas in male participants.

Conclusion: MIRACLE is the largest, randomized, controlled trial for chemoprevention with green tea extract. Green tea extract taken bid over 3 years was well tolerated and had overall a moderate chemopreventive effect on colorectal adenomas. Green tea extract prevents significantly colorectal adenomas in males but not in females pointing to a gender specific difference in chemoprevention. This effect seems to have an impact especially to the recurrence of low-grade adenomas. Further subgroup analyses and translational research are ongoing.

Disclosure: Nothing to disclose

P0726

MANAGEMENT OF SERRATED POLYPOSIS SYNDROME FROM THE VIEWPOINT OF LONG-TERM OBSERVATION

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Introduction: Serrated polyposis syndrome (SPS) is colorectal polyposis syndrome characterized by accumulation of serrated lesions and serrated adenomas, and known with greater risk of colorectal carcinoma (CRC). However, the benefit of endoscopic surveillance and treatment for SPS has been unclear.

Aims & Methods: This study aimed to clarify the clinicopathological features and prognosis for SPS in relation to the surveillance. We extracted patients corresponding to the 2014 WHO SPS diagnostic criteria (i: At least five serrated polyps proximal to the sigmoid colon, two of which are ≥ 10 mm in diameter, ii: Any number of serrated polyps occurring proximal to the sigmoid colon in an individual who has a first-degree relative with serrated polyposis, iii: More than 20 serrated polyps of any size distributed

throughout the colon) treated between January 2008 and December 2019 from the endoscopy database of Hiroshima University Hospital. We examined their clinicopathologic characteristics, treatment outcome, and prognosis. For SPS cases in our department, all lesions with a diameter ≥ 10 mm or suspected of being cancer were endoscopically resected. Surveillance colonoscopy was performed once a year on principle.

Results: Of the 54,633 patients who underwent colonoscopy, 28 (0.051%) met the criteria for SPS. Mean age at diagnosis was 56.5 (32-76) years and 15 (57%) were men. Resected lesions in the observation period were 282 overall, 191 (68%) in the right colon, 77 (26%) in the left colon, 14 (5%) in the rectum, and 7.5 (2-34) per case. The mean size of the largest tumor in each case was 20 ± 11 (12-50) mm. The breakdown of histological types for all resected lesions was 47 cases (17%) of hyperplastic polyps, 146 (52%) of sessile serrated lesion, 35 (12%) of serrated adenoma, 45 (16%) of tubular adenoma, 2 (0.7%) of tubulovillous adenoma, 3 (1%) of Tis cancer, 2 (0.7%) of T1 cancer, and 2 (0.7%) of T3 cancer. Of 7 carcinoma cases, Narrow Band Imaging magnifying observation of the cancerous part was JNET Type 1 in 1 case (20%), Type 2B in 4 (60%), and Type 3 in 2 (20%). Conversely, pit pattern of the cancerous part was Type II in 1 case (20%), Type III_L in 2 (40%), Type IV in 1 (20%), and Type V in 3 (20%). Endoscopic resection (ER) was performed in 280 of 282 lesions (99%); 270 of 280 lesions (96%) were resected by en bloc. No postoperative bleeding occurred; delayed perforation was observed in 2 cases of ER, however, was cured conservatively. Of 28 SPS patients, 13 were followed up for ≥ 5 years (mean 90 ± 89 months). In these patients, 54 metachronous multiple lesions were detected an average of 30.5 months after treatment; an average of 4 lesions (0-12 lesions) per patient were observed. One of the 54 metachronous multiple lesions was Tis cancer. One of the 13 was a cancer-specific death case. In the fatal case ER was performed for a lesion in the sigmoid colon. Pathological findings of this lesion were tub1> tub2> por, pT1b (SM 2000 μ m), INFc, Ly0, V0, BD2, pHM0, pVM0. This patient underwent surveillance colonoscopy every year at our hospital without additional surgery because of her will, and no recurrence was found for 4 years after ER. In the 5th year after ER, CT examination was performed because an increase in tumor markers was observed and multiple liver metastases were detected. The patient was treated with chemotherapy, however, died 60 months after ER.

Conclusion: Our management of SPS (ER for the lesions with ≥ 10 mm in diameter and annual surveillance colonoscopy after ER) is considered valid.

Disclosure: Nothing to disclose

P0727 WITHDRAWN

P0728

IMMUNOLOGICAL MICROENVIRONMENT IN RECTAL ADENOCARCINOMA TREATMENT (IMMUNOREACT) PRELIMINARY RESULTS: HIGH PD-L1+ CELL INFILTRATION IN HEALTHY MUCOSA IS ASSOCIATED TO NODAL METASTASIS IN EARLY RECTAL CANCER

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Introduction: Transanal local excision has recently received attention as an alternative to radical surgery for early rectal cancer [1]. However, to minimize the recurrence rate after local excision of rectal cancer, the false-negative rate of nodal staging should be minimized [2]. In early rectal cancers absence of CD8+ T-cell infiltration helps in predicting patients' nodal involvement [3]. Field cancerization occurs in various epithelial carcinomas, including rectal cancer, which indicates that the molecular events in carcinogenesis might occur in normal tissues extending from tumors [4].

Aims & Methods: Our aim was to predict the presence of nodal metastasis in patients with early rectal cancer.

In this retrospective and exploratory analysis of FFPE, slides of healthy rectal mucosa surrounding the cancer were retrieved from the pathology archives to test a panel of molecular markers of immune reaction to the cancer (antigen presenting cell and T lymphocyte activation). Patients with pTis, pT1 and pT2 rectal cancers and no previous neoadjuvant therapy were enrolled. Clinicopathologic features and the immunological markers were compared between patients with and without the presence of nodal metastasis that will be assessed by examination of the operative specimen (in case of anterior resection or Miles abdominoperineal resection) or by occurrence of nodal recurrence within one year after trans anal procedures.

Results: In the IMMUNOREACT retrospective cohort, 519 patients were enrolled and 123 of them had pTis, pT1 and pT2 rectal cancers. In this group, 29 patients had nodal metastasis. In healthy rectal mucosa CD3+, CD4+ and CD8+ T cell infiltration was similar in patients with nodal metastasis and in those without nodal metastasis. On the contrary, PD-L1+ cells infiltration of healthy rectal mucosa was higher in patients with nodal metastasis (p=0.05).

Conclusion: Our data suggest that high PD-L1+ cell infiltration in the healthy rectal mucosa surrounding the tumor may favor the immune escape and the passage of cancer cells through lymphatics vessels to lymph nodes. These data might be useful to plan a local excision in early rectal

cancer minimizing the risk of unreckoned nodal metastasis. Analyzing the normal rectal mucosa might overcome the difficulty to obtain adequate tissue sample from a small early cancer.

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Disclosure: Nothing to disclose

P0729

IMMUNOLOGICAL MICROENVIRONMENT IN RECTAL ADENOCARCINOMA TREATMENT (IMMUNOREACT) PRELIMINARY RESULTS: T CELL INFILTRATION OF HEALTHY RECTAL MUCOSA AFTER COMPLETE RESPONSE TO NEOADJUVANT THERAPY IS SIGNIFICANTLY LOWER IN MALES

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Introduction: Some patients with rectal cancer who receive neoadjuvant chemoradiotherapy (nCRT) achieve a pathologic complete response (pCR) and might be eligible for less radical surgery or non-operative management [1,2]. A low stromal Foxp3(+) cell density was observed in 84% of patients who had a pCR compared to 41% of patients who did not [3]. Field cancerization concept indicates that the molecular events in carcinogenesis might occur in normal tissues extending from tumors [4]. The signaling governed by IFN type I has emerged as pivotal in orchestrating host defense against cancer and this pathway displays different activation between sexes [5].

Aims & Methods: Our aim was to identify, among locally advanced rectal cancer, those with immediate and sustained complete response to nCRT analyzing the immune microenvironment in healthy mucosa with a particular focus on possible gender differences.

In this retrospective and exploratory analysis of FFPE, slides of healthy rectal mucosa surrounding the tumor site were retrieved from the pathology archives to test a panel of molecular marker of immune reaction to the cancer (antigen presenting cell and T lymphocyte activation). Clinicopathologic features and the immunological markers were compared between patients with and without pathological complete response to neoadjuvant therapy (TRG1 vs TRG4-5).

Results: In the IMMUNOREACT retrospective cohort, 519 patients with rectal cancer were enrolled and 135 underwent to nCRT. In this group, 25 patients obtained a pCR. No difference in the frequency of pCR was observed in males vs. females ($p=0.73$). However, CD3+, CD4+ and CD8+ T cell infiltration in the healthy rectal mucosa was significantly lower in males with pCR with respect to those who had not a pCR ($p=0.05$, $p=0.06$ and $p=0.03$, respectively). Such difference was not observed among females.

Conclusion: Our data suggest that the immune mediated response to the neoadjuvant therapy may be gender related. In males, the direct effect of nCRT may be more enhanced and in may somehow affect the T cell infiltration of the rectal mucosa. These data might be useful to plan a gender oriented nCRT scheme. Analyzing the normal rectal mucosa might overcome the difficulty to obtain adequate tissue sample from a locally advanced cancer that got complete response.

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Disclosure: Nothing to disclose

P0730

LOW DOSE ASPIRIN IS ASSOCIATED TO A LOWER FREQUENCY OF NODAL METASTASIS IN COLORECTAL CANCER

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Introduction: Long-term daily use of aspirin has been associated with reduced colorectal cancer incidence and mortality [1]. Moreover, among long-term CRC survivors, regular use of aspirin after CRC diagnosis was significantly associated with improved survival in individuals with KRAS wild-type tumors [2].

Aims & Methods: To explore these association, we compared tumor microenvironment, mutational status and nodal metastasis frequency among aspirin users with those among non-users. In this retrospective study, clinical and pathological records of a series of consecutive CRC patients operated on from 2015 to 2019 were retrieved. We considered as aspirin users' patients who started low dose aspirin therapy at least 1 year before the CRC onset. Histology for intratumoral lymphomonocytes infiltration, immunohistochemistry for MLH1, PMS2, MSH2 and MSH6 and mutational analysis of BRAF, KRAS and NRAS were performed. Sporadic CRC and metachronous CRC were compared. Nonparametric tests were used for small sample size comparison.

Results: From 2015 to 2019, 238 patients were operated on for CRC at the General Surgery Unit of the Azienda Ospedaliera di Padova. Among these patients, we identified 29 aspirin users. No difference was observed in term of T stage frequency between aspirin users and non-users, but nodal metastasis was significantly less frequent among aspirin users ($p=0.008$). Similarly, G stage was significantly lower in aspirin users compared to non-users ($p=0.02$).

Moreover, neutrophil to lymphocytes ratio was significantly lower in aspirin users ($p=0.042$). Mismatch repair genes defects and MSI frequency was similar in aspirin users and in non-users ($p=0.31$). However, in MSS patients the number of metastatic lymph nodes was significantly lower in aspirin users than in non-users ($p=0.022$) and the different type mutation of KRAS was different in the two groups ($p=0.008$).

Conclusion: Our study showed that, low dose aspirin was associated, at the same T stage, to a lower frequency of nodal metastasis. Moreover, our data suggest that low dose aspirin therapy is associated to a peculiar the mutational pattern of KRAS in MSS CRC.

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Disclosure: Nothing to disclose

P0731

METACHRONOUS COLORECTAL CANCER HAVE SIMILAR MSI FREQUENCY BUT HIGHER FREQUENCY OF ABSENT LYMPHOMONOCYTES INFILTRATION THAN PRIMARY ONES

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Introduction: An increased risk of metachronous colorectal cancer (CRC), is usually associated to microsatellite instability (MSI) occurring in Lynch syndrome. However, not all the patients with metachronous CRC have MSI. The density of tumor-infiltrating lymphocytes (TIL) is an independent predictor of outcome in patients with colorectal cancer and a fascinating hypothesis is that they can be involved in metachronous CRC onset.

Aims & Methods: The aim of this study was to analyze the tumor microenvironment and tumor mutation frequency in sporadic and metachronous CRC. In this retrospective study, clinical and pathological records of a series of consecutive CRC patients operated on from 2015 to 2019 were retrieved. We considered as metachronous a second CRC arising at least 1 year after the primary one and sporadic CRC those without any metachronous CRC. Histology for intratumoral lymphomonocytes infiltration, immunohistochemistry for MLH1, PMS2, MSH2 and MSH6 and mutational analysis of BRAF, KRAS and NRAS were performed. Sporadic CRC and metachronous CRC were compared. Nonparametric tests were used for small sample size comparison.

Results: From 2015 to 2019, 238 patients were operated on for CRC at the General Surgery Unit of the Azienda Ospedaliera di Padova. We identified 26 metachronous CRC patients. No difference was observed in term of cancer stage between metachronous and sporadic CRC. Mismatch repair genes defects and MSI frequency was similar in metachronous CRC and in sporadic CRC ($p=0.77$). Similarly, mutation frequency of BRAF and KRAS was similar in the two groups ($p=0.75$ and $p=0.21$, respectively). On the contrary, patients with metachronous CRC had a higher frequency of absent lymphomonocytes infiltration within the tumor ($p=0.004$) and they tended to have a higher frequency of NRAS mutation ($p=0.06$).

Conclusion: Our study showed that, rather unexpectedly, MSI frequency was similar in metachronous and sporadic CRC. Moreover, our data suggest that an altered immune microenvironment may be a crucial factor permitting the occurrence of a metachronous CRC. In fact, absent lymphomonocytes can be the substrate for a weak immune response to cancer neoantigens that can open the way to a second primary CRC.

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Disclosure: Nothing to disclose

P0732 WITHDRAWN

P0733

PT1 COLORECTAL CANCER DETECTED IN A POPULATION BASED COLORECTAL CANCER SCREENING PROGRAMS: TREATMENT AND FACTORS ASSOCIATED WITH RESIDUAL OR ADVANCED DISEASE

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Introduction: Colorectal cancer (CRC) screening programs reduce CRC mortality through the detection of CRC at earlier stages and increases the number of pT1 CRC patients treated endoscopically.

Aims & Methods: The aim of this study is to describe the management of pT1 in a CRC screening program, the side effects related to surgical treatment and the factors associated to residual colonic disease, lymph node involvement or recurrence. We included in this retrospective analysis all the pT1 CRC detected in the Galician CRC screening program between May 2013 and June 2019.

We performed a descriptive analysis regarding the demographic characteristics, the location, size, morphology, endoscopic and surgical treatment and the histological findings. We determined which variables were associated with residual disease (local, lymph node, recurrence) in those patients treated endoscopically. Finally, we determined which variables were associated with advanced disease (lymph node, recurrence) in the patients who underwent surgery.

Results: In the study period, 971 CRC (TNM I= 49.6%, II= 19.2%, III= 25.3%, IV= 5.9%) were detected. 370 patients were pT1 (354 pT1 NX-0, 16 pT1N1) and were included in the analysis. 277 (74.9%) were initially resected endoscopically and 162 (43.8%) were not referred to surgery. In the seven endoscopy units participating in the CRC screening program, the rate of initial endoscopic resection ranged between 46.7% and 83.7% (p=0.01). The rate of surgery after the endoscopic resection ranged between 14.3% and 56.5% (p=0.1). The global surgery rate ranged between 45.5% and 72.6% (p=0.05). The complications among patients that underwent surgery (208) were minor in 10.3%, major in 4.6%, the mean stay was 9.6±11.9 days and there was no death. After discharge, surgery related complications were

detected in 34 (16.3%) patients. In the patients treated endoscopically without subsequent surgery (162), there was no recurrence detected after 25.7±13.4 months. In the patients that underwent surgery after endoscopic resection (115), residual colonic disease and lymph node involvement were detected in seven (6.1%) and five (4.3%) patients, respectively. No recurrence was detected after 30.4±15.7 months.

Finally, in the patients that underwent direct surgery (93), a lymph node involvement and a recurrence was detected in eleven (11.8%) and two (2.2%) patients after 29.0±15.2 months. The factors associated with residual disease after endoscopic treatment were non-pedunculated lesion (7.8%, 2.3%; OR 3.6, 95% CI 1.05-12.2), well differentiated lesion (3.5%, 14.3%; OR 0.22, 95% CI 0.05-0.88), infiltrated or non-evaluable resection border (14.8%, 1.4%; OR 12.3, 95% CI 3.2-47.0) and Haggitt 4 (8.8%, 0.8%; OR 11.7, 95% CI 1.4-94.1). On the other side, the factors associated with residual disease after surgical treatment were endoscopic resection (4.3%, 14.0%; OR 0.28, 95% CI 0.09-0.82) and well differentiated histology (6.5%, 20.6%; OR 0.26, 95% CI 0.09-0.74).

Conclusion: pT1 CRC account for a relevant proportion of cancers detected within CRC screening programs and most of these patients are candidate for endoscopic treatment. Although surgery is a safe procedure, we need more accurate criteria to identify those patients with a low risk of residual disease after endoscopic treatment.

Disclosure: Nothing to disclose

P0734

IS THERE PLACE TO EXCLUSIVE ENDOSCOPIC RESECTION FOR HIGH RISK MALIGNANT COLORECTAL POLYPS?

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Introduction: Endoscopically resected malignant colorectal polyps have a significant risk of residual cancer in the bowel wall and lymph nodes that depends on non-uniform histological features.

Aims & Methods: Our aim was to evaluate the frequency of unfavorable histologic features and their relation with residual cancer in the bowel wall and/or lymph nodes.

Single centre prospective cohort study including high risk malignant colorectal polyps endoscopically resected between 2013 and 2019. Malignant polyps were classified as high risk if one or more the following criteria were present: poor differentiation; piecemeal resection; invasion depth >1 mm, that is, Haggitt 4 in pedunculated tumors and Kikuchi 2/3 in non pedunculated tumors; lymphovascular invasion; tumor budding; resection margins positives or cannot be assessed. High risk malignant colorectal polyps were submitted to additional surgical resection, unless there were contraindication or patient refusal. Demographic, endoscopic and histologic characteristics were analysed.

Results: There were 93 patients included, 67% (n=62) males with a median age of 66 (58-74) years of age. The median size of lesions was 15 mm (11-24) mm and 50% (n=46) were located at sigmoid colon. Piecemeal resection was performed in 23% (n=21), tumor budding was present in 40% (n=37), invasion depth >1mm in 62% (n=58), resection margins positives or non-determined in 42% (n=39), lymphovascular invasion in 10% (n=9), poor differentiation in 6% (n=6), Haggitt 4 in 3 (3.2%) and Kikuchi 2/3 in 20.4% (n=19). In 57% (n=53) lesions, additional surgery was performed, of those 72% (38/53) have no residual cancer or lymph nodes involvement. Lesions with residual cancer in the bowel wall and/or lymph nodes involvement had more unfavorable features (3 vs. 2, p<0.01). In multivari-

ated analyse, lymphovascular invasion (OR:16; CI95%:1.5-176) and Haggitt 4 (OR:1.004; CI95%:1.001-1.01) were associated with residual cancer in the bowel wall and/or lymph nodes.

Conclusion: According to previous studies, most malignant colorectal polyps endoscopically resected show no residual cancer in the bowel wall or in lymph nodes. In our cohort, patients with just two unfavorable features, not including lymphovascular invasion or Haggitt 4, additional surgery can be dispensable. More studies are necessary to validate our results.

Disclosure: Nothing to disclose

P0735 WITHDRAWN

P0736

MALIGNANT POLYPS MANAGEMENT - A COHORT STUDY

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Introduction: Malignant polyps (MP) are polyps with invasive cancer into the submucosa. The management of a MP following endoscopic removal is difficult because of the possibility of residual malignant disease. Treatment decision (surveillance vs surgery) remains a challenge as the number of MP removed endoscopically keeps rising.

Aims & Methods: Single center retrospective study evaluating oncologic outcomes of a cohort of patients referred to a colorectal cancer (CRC) multidisciplinary team after endoscopic resection of MP between 2010-2018. Clinical, endoscopic and histological features were analyzed.

High risk features (HRF) for residual cancer defined as resection margin <1mm, poor differentiation, incomplete or piecemeal resection, lymphovascular invasion.

Results: A total of 120 patients were included (male: 65.0%; age - 64.5±10,6 years; follow-up: 26.8±16.4 months).

MP occurred mainly in the sigmoid and rectum (83,4%), measured ≥10mm in 87.5% of cases and 68,3% were sessile or flat. Complete endoscopic removal achieved in 80%; en bloc resection carried out in 69.2%. Histological characteristics (some data missing in 7 patients): 83 patients had resection margin <1mm, 5 had lymphovascular invasion and 6 had poor differentiation. Overall, 76.7% (n=92) of patients had at least one HRF.

For the 23,3% low risk MP, surveillance was recommended. During follow up, no patient had CRC recurrence and one patient died (unknown cause). Surgery with lymph node dissection was proposed to 63 patients with at least one HRF, but 3 patients refused. In the remaining 29 patients with at least one HRF [margin< 1mm (n=21); piecemeal resection (n=8)], surveillance was proposed. The reasons were: margin close to 1mm (n=6), advanced age/comorbidities (n=5), low rectal location (n=12), polypectomy scar not found (n=3), polypectomy>12 weeks before referral (n=3). Twelve patients with rectal MP received therapy before surveillance: 4 received chemoradiotherapy (CRT); 8 underwent transanal resection of the polypectomy scar area (no residual cancer found in any of them).

In patients with at least one HRF, there were 3 CRC recurrences and 3 deaths due to CRC or unknown cause. There were no statistical significant differences in recurrence rate or death from CRC or unknown cause between patients that underwent surgery and patients who were surveilled (p=0.276, for both), even when patients who received therapy before surveillance were excluded.

In the 6 patients with no tumor in the resection margin but margin < 1mm, there were no recurrences and 1 death from an unknown cause.

In patients who underwent surgery (n=60), residual malignant disease was identified in the surgical specimen in 25% (bowel wall - n=10, positive lymph nodes - n=6, both - n=1). Univariate analysis showed incomplete endoscopic resection was significantly associated with the presence of residual cancer in the bowel wall (p=0.025). Multivariate analysis including only patients with complete data showed lymphovascular invasion was associated with presence of residual tumor in the bowel wall and/or lymph nodes (p=0.042) and with positive lymph nodes alone (p=0.047). None of the other HRF were significantly associated with the presence of residual tumor, occurrence of recurrence or mortality.

Conclusion: In our cohort, incomplete endoscopic resection and lymphovascular invasion were the only HRF that significantly determined the presence of residual tumor in the surgical specimen. A clear resection margin, even if < 1mm may be oncologically safe.

Disclosure: Nothing to disclose

P0737

RISK FACTORS OF RECURRENCE AMONG T1 COLORECTAL CANCERS TREATED BY ENDOSCOPIC RESECTION OR SURGERY WITH LYMPH NODE DISSECTION

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Introduction: The recurrence of T1 colorectal cancers is relatively rare. Although some cases develop recurrence after resection, their prognostic factors still remain obscure.

Aims & Methods: The aim of this study is to clarify the risk factors for recurrence in patients with T1 colorectal cancers treated by endoscopic resection (ER) alone or surgical resection (SR) with lymph node dissection. We analyzed 1034 patients with T1 colorectal cancers resected endoscopically or surgically at our center from April 2001 to December 2016, and followed them up over a mean period of 51.6 months. We divided the patents into two groups: endoscopic resected (ER) alone group (394 cases), and surgically resected (SR) group (640 cases). Recurrence-free survival was compared between the ER and SR groups using the Kaplan-Meier method and the log-rank test. The association between recurrence and clinicopathological features was also analyzed using the Cox regression analysis.

Results: The recurrence was recognized in 4 (1.02%) cases in the ER group and 7 (1.09%) cases in the SR group, and there was no statistical difference by log-rank test. The Cox regression analysis showed that lesions located in the rectum and lesions with poorly differentiated adenocarcinoma or mucinous carcinoma (Por/Muc) were the contributor to recurrence in both ER and SR groups. In addition, female sex, depressed lesions and lymphatic invasions were also the risk factors of recurrence in the ER group but not in the SR group.

Conclusion: The prognostic factors for recurrence in patients with T1 colorectal cancers were rectal location and Por/Muc differentiation. Surgery with lymph node resection could reduce the risk of recurrence in patients with lymphatic invasion, depressed-type morphology or female sex.

Disclosure: Nothing to disclose

P0738

ADJUVANT FULL-THICKNESS RESECTION AFTER ENDOSCOPICALLY REMOVED T1 COLORECTAL CARCINOMA WITH UNCERTAIN RADICALITY BUT WITHOUT OTHER RISK FACTORS FOR LYMPH NODE METASTASIS: IS IT ONCOLOGICALLY SAFE?

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Introduction: Local full-thickness colorectal wall resections (FTR) of scar tissue is increasingly used as completion therapy for endoscopically removed T1 colorectal carcinomas (CRCs) with irradical (R1) or uncertain (Rx) resection margins, but absence of other histological risk factors (lymphovascular invasion (LVI) or poor differentiation). If the locally resected bowel wall shows no intramural residual cancer, an adjuvant surgical resection (ASR) is considered unnecessary. However, the risk of leaving locoregional lymph nodes in situ has not been evaluated. We investigated the presence of lymph node metastasis (LNM) in ASR specimens showing no intramural residual cancer after endoscopically resected R1/Rx T1 CRC.

Aims & Methods: Data on patients treated for T1 CRC between 2000 and 2018 were collected in 24 Dutch hospitals and included polyp characteristics (size, location, morphology), type of endoscopic resection, histo-

logical assessment, type of surgery and patient characteristics. Eligibility criteria for this study were: 1) a macroscopically radical endoscopic resection; 2) Rx/R1 or R0 ≤ 1 mm; 3) absence of LVI and poor differentiation; and 4) treatment with ASR. Endpoint was the presence of LNM or residual cancer in the scar. All cases with LNM were reviewed by an expert gastrointestinal pathologist (histological risk factors and resection margins on the hematoxylin-eosin staining slides of the original specimen). Subgroup statistical analysis was performed with Chi-squared test.

Results: Of 3287 patients with a T1 CRC, 376 met all the inclusion criteria (mean age 66 years, ASA I-II 87%, 43% female). In 23/376 (6.1%) patients, residual cancer was detected in the scar, of whom 4/23 (17%) also had LNM. Of the remaining 353 patients without intramural residual cancer, 30 (8.5%) showed LNM. The risk of LNM was 5.8% in patients treated between 2000 and 2014, and 10.3% in patients treated between 2014 and 2018. However, data on LVI was missing in 68% and 8%, respectively. The risk for LNM was similar for rectum and colon tumors (7.9% vs. 9.5%, p=0.540), and piecemeal vs. en bloc resection (7.8% vs. 9.8%; p=0.750). Histological review could be performed in 24/30 LNM cases without residual cancer in the scar and showed LVI and/or poor differentiation in 17 cases (71%). If high-grade tumor budding is added as risk factor, 21 cases (88%) are defined as high-risk for LNM, one as low-risk and two remain with an unknown risk. Finally, to study if these results can be extrapolated to patients undergoing FTR, we compared baseline characteristics to a FTR only group of 153 patients (mean age 67 years, ASA I-II 86%, 41% female). There was no difference in age (p=0.460) and ASA classification (p=0.781) between both groups that could explain the unexpected high frequency of LNM in the ASR group. Furthermore, distribution of en-bloc resection (61% vs. 58%, p=0.589) and mean polyp size were also comparable (20.1 vs. 20.8 mm, p=0.368). However, the ASR group showed significantly more T1 CRCs located in the colon. Residual cancer was detected in the scar in 12.4% of the cases.

Conclusion: T1 CRC with an R1/Rx resection margin without LVI or poor differentiation is associated with a significant (9%) risk of LNM. The majority could be explained by unidentified histological risk factors. Completion FTR should therefore be preceded by double reading of the pathology and accompanied with intensive follow-up.

Disclosure: Nothing to disclose

P0739 WITHDRAWN

P0740

INFLUENCE OF LIVER STEATOSIS ON DEVELOPMENT OF LIVER METASTASIS IN RECTAL CANCER PATIENTS SUBMITTED TO NEOADJUVANT CHEMORADIOTHERAPY AND CURATIVE RESECTION

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Introduction: The liver is the most frequent site of distant metastasis of colorectal cancer and liver metastasis are one of the main prognostic factors in these patients. Recent studies have shown that hepatic microenvironment is an important factor in the development of metastasis. Nevertheless, the role of hepatic steatosis (HS) in the incidence of liver metastases from colorectal cancer is not well established.

Aims & Methods: The aim of this study was to evaluate a possible link between HS and liver metastases in patients with rectal cancer that underwent neoadjuvant chemoradiotherapy (nCRT) and curative resection. Patients diagnosed with rectal carcinoma from March 2012 to September 2018, who underwent nCRT and curative resection were included. The mean attenuation values of liver and spleen on pre-treatment computed tomography (CT) were obtained in Hounsfield Units and HS was assumed in all patients with a liver-to-spleen ratio lower than 1.0.

Results: Among 108 patients with rectal cancer that underwent nCRT and curative surgery, we excluded all cases without noncontrast CT prior to treatment, therefore a total of 98 patients were included in this study. Fifty-seven (58.2%) were male and mean age was 64.3 ± 10.1 years. Eighty-seven (88.8%) had locally advanced carcinomas. Thirteen (13.3%) had HS according to radiologic criteria. The mean duration of follow-up from surgery to the last in-hospital medical evaluation/death was 33.1 months (± 18.7). Twelve patients (12.2%) developed liver metastasis during follow-up. The incidence of liver metastasis was significantly higher in patients with HS ($p = 0.009$) and lower in patients with downstaging ($p = 0.032$) or a complete pathologic response ($p = 0.035$) after nCRT. Body mass index did not influence the incidence of liver metastasis ($p = 0.489$). No statistically significant differences were found on the incidence of extrahepatic metastasis between patients with or without HS ($p = 0.176$). On multivariate analysis, HS was an independent risk factor for the development of liver metastasis (odds ratio = 4.84; 95% confidence interval: 1.12-20.95, $p = 0.035$).

Conclusion: Liver metastases from rectal cancer are more common in HS which may suggest that HS can be a favourable microenvironment for development of liver metastasis. These results raise the question if a therapeutic intervention in HS may reduce the incidence of liver metastases and increase survival of patients with rectal carcinoma.

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Disclosure: Nothing to disclose

P0741

MACHINE LEARNING MODEL TO PREDICT THE RISK OF COLORECTAL CANCER AMONG KOREAN GENERAL POPULATION: RESULTS FROM TWO NATIONWIDE LONG-TERM FOLLOW UP STUDIES

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Introduction: While emerging evidences have been stack on the association of un-healthy life style and the risk of colorectal cancer (CRC), there has been limited data on the prediction model for colorectal cancer among general population considering comprehensive life style factors.

Aims & Methods: We aimed to develop machine learning (ML) algorithm based CRC prediction model using two nationally representative long-term follow up cohorts in Korea. We used nationally representative two

cohort studies, CardioVascular Disease Association Study (CAVAS) and Korean Health Examinee Study (HEXA) which goals were to investigate the association of life style and the risk of common complex diseases such as CRC in Korea. Data from CAVAS ($n=28337$, baseline data: 2005-2011, follow up data: 2007-2016) study was used for training/test set and HEXA study ($n=173209$, baseline data: 2005-2013, follow up data: 2007-2016) was for external validation set to develop and validate ML based CRC prediction model for general population. Main outcome was defined as the incident CRC (time-varying exposure) during follow up period among population who aged over 40 years and ever had colonoscopy. Variables included life style factors (diet pattern, physical activity, smoking, and drinking), stress perception, anthropometric indices, medical history, medication history, family history of CRC, previous history of colon polyp, and socioeconomic factors. ML algorithms included support vector machine, random forest, artificial neural network, XGBoost, and ensemble methods. Area under receive operating curves (AUROC) of each methods were compared.

Results: After exclusion of baseline CRC history, and no data on follow up study, during 766717 person-year, total of 219 new incidental colon cancer cases were included in final cohort. In external validation using HEXA study, ML model of Ensemble method for prediction of CRC yielded area under receive operating curve (AUCs) of 0.85 (95% confidence interval (CI) 0.80 to 0.90) adjusting for life style factors (diet pattern, physical activity, smoking, and drinking), stress perception, anthropometric indices, medical history, medication history, family history of CRC, previous history of colon polyp, and socioeconomic factors, and followed by XGBoosts model which showed AUROC of 0.82 (95% CI 0.80 to 0.85)).

Conclusion: In this large nationwide prospective Korean cohort, ML based prediction model of CRC development among population aged over 40 years showed good predictive function in external validation cohort with comprehensive life style factors, and enable physicians to close follow up based on personal lifestyle based estimation though ML algorithm.

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P0742

TTA-121, A NOVEL OXYTOCIN NASAL SPRAY, IMPROVES ABDOMINAL PAIN IN A RAT IRRITABLE BOWEL SYNDROME MODEL

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Introduction: Irritable bowel syndrome (IBS) is a chronic illness characterized by increased abdominal pain, bloating and discomfort associated with a change in bowel habits. Oxytocin is a peptide hormone produced in the paraventricular nucleus and supraoptic nucleus of the hypothalamus and released by the posterior pituitary. It promotes the parturition and suckling and plays an important role in prosocial behaviors. Recently,

we demonstrated that TTA-121, our oxytocin nasal spray, attenuated repeated cold stress-induced tactile allodynia in a rat fibromyalgia model. In this study, we examined an analgesic effect of oxytocin on abdominal pain using IBS model rats.

Aims & Methods: Rats were exposed to restraint stress for 1 hour in the restraint stress cages (4.5 × 4.5 × 18.0 cm), whereas sham-operated rats were placed in home cages. During restraint stress exposure, the number of feces was counted. Then, barostat catheters were inserted into the colon of rats and the rats were habituated to the catheters for 30 minutes. After the habituation, the catheters were inflated to a pressure of 60 mmHg and the number of abdominal muscle contractions was counted for 5 minutes. 1 hour before the restraint stress exposure, rats received an intranasal treatment of vehicle or oxytocin formulation (TTA-121, 25 µL/body, Teijin Pharma Ltd.), or an oral treatment of ramosetron, a commercially available drug for IBS.

Results: The number of abdominal muscle contractions and feces were significantly increased by restraint stress exposure. Ramosetron significantly improved stress-induced abdominal pain and abnormal defecation. Furthermore, TTA-121 completely inhibited the number of stress-induced abdominal muscle contractions, but not the number of feces.

Conclusion: This study shows that TTA-121 improves abdominal pain in IBS model. Our intranasal oxytocin formulation is expected to be a novel therapeutic option for IBS.

Disclosure: Nothing to disclose

P0743

INTAKE OF A PROBIOTIC MIXTURE INCLUDING *BIFIDOBACTERIUM LONGUM*, *LACTOBACILLUS HELVETICUS* AND *LACTOBACILLUS PLANTARUM* AFFECTS BRAIN ACTIVITY AND STRESS RESPONSE IN HEALTHY SUBJECTS: POTENTIAL IMPACT ON GUT-BRAIN AXIS DISORDERS

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Introduction: The gut-brain axis is a bidirectional communication system which is disturbed in disorders such as irritable bowel syndrome. Few clinical studies in healthy subjects have shown that probiotic intervention might affect brain activity and behaviour.

Aims & Methods: This study assessed how a probiotic intervention containing *Bifidobacterium longum* R0175, *Lactobacillus helveticus* R0052 and *Lactobacillus plantarum* R1012 affects the microbiota-gut-brain axis.

In this double-blinded, placebo-controlled crossover study, 22 healthy subjects (age 24 ± 3 years, 6 male/ 16 female) were exposed to a probiotic intervention (15 × 10⁹ CFU/day) and a placebo in randomised order for 4 weeks each, separated by a 4-weeks wash out. To assess the effect of the probiotic on brain function, subjects underwent functional magnetic resonance imaging, fMRI (GE Discovery 750w 3T, acquired voxel size 3.74 × 3.75 × 4 mm, temporal resolution 2.5 sec), while performing an emotional attention task (EAT) and an arithmetic stress task (MIST) after each intervention period. The interventions were compared with respect to differential activity evoked by the challenge paradigms (using R) and with respect to differential connectivity (using CONN). Stress-inducing effects of the fMRI paradigms were assessed by salivary cortisol. Blood was analysed for initial evaluation of the mode of action via which the probiotic affects the gut-brain axis. Psychological symptoms were assessed by questionnaires (HADS, STAI, PSS). Order of intervention was considered for statistical analysis.

Results: Altered brain responses, measured as blood-oxygenation-level-dependent (BOLD) changes, were observed in brain regions (based on BNA regions) implicated in the processing of emotion, cognition, memory and emotional faces when comparing emotional challenge to control condition. The response pattern, defined as contrast between those conditions, was altered after probiotic intervention compared to placebo, with increased activity in some brain regions and decrease in others (exploratory whole brain analysis). Literature-based predefined regions of interest (ROI, n=31) were statistically overrepresented (p < 0.001) in the set of regions with significantly altered activity (11 ROI among 18 regions with p < 0.1). An exploratory seed-to-voxel analysis revealed slight differences in functional connectivity evoked by EAT between both interventions. The probiotic also affected the brain response pattern during MIST, but this was not significant after Bonferroni correction nor was any of the regions among the predefined ROIs. Salivary cortisol levels were increased during the course of the fMRI measurements with a peak during MIST. Generally, salivary cortisol was significantly increased by 0.51 nmol/l (after subtraction of carry-over effects) after probiotic intervention compared to placebo. Brain derived neurotrophic factor (p=0.12) and serotonin (p=0.08) in serum were not significantly differentially affected by the probiotic. Self-rated stress, depression and anxiety scores did not differ significantly between the interventions.

Conclusion: The probiotic intervention evoked distinct changes in brain activity and stress response in healthy subjects performing specific tasks. These results give important hints how patients with a disturbed gut-brain axis function could benefit from probiotic intake. Further analysis of signalling molecules could give possible insights into the mode of action of the probiotic intervention on the microbiota-gut-brain axis in general and brain function specifically.

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P0744

INCONGRUENT VIEWS OF QUALITY OF LIFE BETWEEN PATIENTS AND GASTROENTEROLOGISTS: A MIXED-METHODS ENQUIRY

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Introduction: Functional Gastrointestinal Disorders (FGIDs) are disorders of brain-gut interaction that result from a combination of motility disturbance, visceral hypersensitivity, altered mucosal, immune function, altered gut microbiota and central nervous system processing. The objective of the present study was to examine the relationship between incongruence, which was defined as a differing perception of the illness between the patient and the physician, and type of diagnosis (functional or organic) with psychopathology.

Aims & Methods: The first part of the research aimed to assess the patient's clinical functioning, as well identify the levels of satisfaction that patients have with the physician. A total of 1,562 patients with gastrointestinal disorders were involved in the first part. Incongruence was calculated as the difference between the clinician-rated functionality (Karnofsky Performance Status Scale) and the subjectively rated quality of life (physical functioning of the SF-36 subscale). Psychopathology was measured by means of scoring the responses given on the Brief Symptom Inventory-18 (BSI-18) and satisfaction with the physician was measured using the Patient-Doctor Relationship Questionnaire (PDRQ-9). The second part of the research aimed to obtain a global picture of the patient's health, as well as gain an insight from gastroenterologists regarding the challenges they face when working with this subgroup of patients. Patients were invited to take part in the qualitative part of the study if they had incongruent views with the physician or were considered as being resilient. The qualitative section of the study involved a total of eight patient focus groups and four physician interviews.

Results: The results indicated that both the presence of incongruent views between the patient and the physician, as well as a functional gastrointestinal diagnosis predict higher levels of psychopathology. Interestingly no interaction was found between the aforementioned variables suggesting that they function independently in psychopathology, thus suggesting that neither of the diagnostic groups had greater levels of incongruence. Whilst both factors contribute to psychopathology, incongruent views between the patient and the physician had a much higher explanatory power on psychopathology than the diagnosis of the patient. During the second part of the study, a total of five themes were identified from the patient focus groups and the physician interviews: Illness-emotional and personal problems; disease-health system interaction; health-system; intervention and patients.

Conclusion: The study has allowed us to identify a psychosocial factor (i.e. incongruence) that may be indicative of lower wellbeing and quality of life.

Disclosure: Nothing to disclose

P0745

GENOME-WIDE ANALYSIS OF 53,400 PEOPLE WITH IRRITABLE BOWEL SYNDROME HIGHLIGHTS SHARED PATHWAYS WITH NEUROAFFECTIVE TRAITS

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Introduction: Despite its high prevalence, the causes of irritable bowel syndrome (IBS) are poorly understood. The relative contribution of gut and brain factors is debated. As IBS has a demonstrated heritable component, identifying genes influencing IBS risk has the potential to provide valuable pathophysiological insights.

Aims & Methods: We developed a digestive health questionnaire for the UK Biobank and combined identified IBS cases and controls with independent cohorts. The discovery dataset comprised 53,400 IBS cases and 433,201 controls with genome-wide data. Significant associations were tested in a replication cohort from 23andMe, Inc. (205,252 cases, 1,384,055 controls).

Results: We identified 6 novel genome-wide significant IBS associations ($p < 5 \times 10^{-8}$), all of which replicated in the 23andMe cohort. Implicated genes include *NCAM1*, *CADM2*, *PHF2/FAM120A*, *DOCK9*, *CKAP2* and *BAG6*. Estimated heritability was modest ($h^2 = 5.8\%$, $SE = 0.35\%$). We found considerable polygenic correlation with neuroaffective traits, including anxiety ($r_g = 0.58$, $SE = 0.10$), neuroticism ($r_g = 0.54$, $SE = 0.04$), depression ($r_g = 0.53$, $SE = 0.05$) and insomnia ($r_g = 0.42$, $SE = 0.05$). We also observed strong phenotypic associations between IBS and neuroaffective traits, along with risk factors such as childhood antibiotic exposure and family history. Additional analyses implicate shared pathways between IBS and anxiety rather than one condition causing the other.

Conclusion: Individual IBS genetic susceptibility loci are shared with neuroaffective traits and implicated in the development of neural circuits. Genome-wide comparisons also highlight the overlap with psychological traits but not with immune or inflammatory intestinal disorders. Overall, these genetic results implicate central neural and psychological mechanisms in IBS development.

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P0746

IMMUNOPHENOTYPING AND FUNCTIONAL CHARACTERIZATION OF NAÏVE MAST CELLS IN IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain and changes in stool pattern. The underlying pathogenesis is still largely unknown, although mast cells (MC) are suggested to play an important role. These MC are heavily influenced by their surroundings and release mediators affecting gut sensitivity in response. Numbers of MC seem to be increased, but results are inconsistent. Therefore, it is suggested that the behavior and activity of MC is important rather than the amount.

Aims & Methods: The aim of this study was to characterize naïve peripheral blood cultured MC with flowcytometry and determine if there is an immunophenotypical and functional difference between IBS and healthy controls (HC). MC were cultured for 5 weeks from CD34⁺ progenitor cells isolated from peripheral blood. Immunophenotypical analysis comprised staining of CD117, CD203c, MRGPRX2, IgE receptor, CD300a and CD32. Functional analysis was performed by staining intracellular calcium and measuring the appearance of the degranulation marker CD63 after stimulation

with substance P, the natural ligand of MRGPRX2, and through an IgE-dependent mechanism with cross-linking of the FcεRI with anti-IgE receptor. Results are presented as median (range). Densities are presented as mean fluorescent intensity (MFI).

Results: MC were defined as CD117+CD203c+ cells. We analyzed cultures of 6 IBS patients and 5 HC. In basal conditions MC of HC and IBS patients display similar surface expression: CD300a, FcεRI and CD32 are all fully expressed on the MC of both groups. MRGPRX2 expression shows a trend however no statistical significance was reached: in IBS patients 48.2% (11.1%-91.24%) and in HC 56.5% (19.9%-78.0%). CD203c has a comparable density of 1674 MFI (1433-2055) in IBS and 1993 MFI (1329-2471) in HC, while CD63 is minimally expressed in resting MC in both groups. After activation with anti-FcεRI and substance P, CD63 appeared in a comparable manner in HC and IBS patients: activation with substance P (after 20 min) resulted in a non-significant appearance of CD63 of 49.4% (8.1%-80.6%) in IBS and 12.8% (8.2%-82.3%) in HC ($p = 0.9307$). Activation with anti-FcεRI (20 min) on the other hand caused a non-significant appearance of 22.9% (10.7%-56.2%) in IBS and 10.3% (4.4%-51.3%) in HC ($p = 0.3290$).

Conclusion: When analyzing naïve peripheral blood cultured MC, we do not find an immunophenotypical or functional difference between MC of IBS patients or HC. As MC are tissue resident cells and thus further differentiate based on their environment, we will try to mimic the GI environment and add supernatant of IBS patients to the MC cultures and investigate its effect on MC differentiation and behavior.

Disclosure: Nothing to disclose

P0747

MAST CELL AND ENTERIC NERVE CHANGES IN IRRITABLE BOWEL SYNDROME PATIENTS WITH AND WITHOUT HYPERMOBILE EHLERS DANLOS SYNDROME

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Introduction: Hypermobile Ehlers-Danlos syndrome (hEDS) is characterized by skin hyperextensibility, tissue fragility and joint hypermobility. hEDS is a multisystemic disorder associated with several comorbidities, including features consistent with irritable bowel syndrome (IBS) (Nelson et al 2015, Zeitoun et al, 2013). In IBS, abdominal pain is associated with heightened colonic sensitivity allied to an increased density of nerve fibres (Akbar et al 2008), and increased expression of mast cells (Barbara et al 2004). Animal studies in Tenascin X knockout mice, which exhibit features similar to hEDS, have similarly demonstrated increased colonic afferent sensitivity with an increased expression of nociceptive CGRP nerve fibres in the colonic mucosa (Aktar et al 2018). Therefore, we hypothesize that there is also an alteration in nerve profile and mast cells in hEDS patients with IBS features; similar to findings in previous IBS studies and in animal models of hypermobility.

Aims & Methods: Our aim was to characterize the molecular changes in the colonic mucosa associated with abdominal pain in IBS alone, and in comorbid IBS/hEDS through the assessment of nerve fiber density (PGP & CGRP) and mast cell expression.

Immunofluorescence-immunohistochemistry (IF-IHC) was used to evaluate expression of mast cell tryptase (AA1 Dako, M7052, 1:400) and the neural markers CGRP (Thermo Scientific ABS 0260502, 1:200) and PGP9.5 (Dako, Z5116, 1:400) in the colonic mucosa of: IBS patients (N=4), and IBS patients with comorbid hEDS (N=4). To determine the presence of positive fibres an approximate threshold of 20% above background (defined as a 0% black image) was used. The positive areas were highlighted to give a

'region of interest;' thereafter the number of pixels in the region of interest were measured. Mast cells were counted on Image J using the multipoint tool. Results were analysed using an unpaired *t*-test for each marker; with a *P*-value < 0.05 deemed significant.

Results: The co-morbid IBS/hEDS group demonstrated a 2-fold proliferation in PGP 9.5 immunoreactive fibers compared to those with IBS alone (comorbid IBS/hEDS: 41476 ± 6196 vs IBS alone 22245 ± 3404 , $p = 0.003$). However, this was not the case for CGRP positive fibers or mast cells which were significantly reduced in hEDS/IBS overlap compared to IBS alone (CGRP: comorbid IBS/hEDS: 329 ± 165 vs IBS alone 1557 ± 559 , $p = 0.015$), (Mast cell tryptase: comorbid IBS/hEDS: 25 ± 3 vs IBS alone 44 ± 5 , $p = 0.001$).

Conclusion: In contrast to animal models of hypermobility, these initial results demonstrate CGRP is very limited in the human colon in hEDS/IBS patients. The two groups demonstrate a distinct difference in neuronal innervation of the gut; with the IBS alone cohort displaying an increase in the expression of specific nociceptive fibers and inflammatory markers. This suggests that different inflammatory/nociceptive pathways may be involved in comorbid IBS/hEDS; signifying the overlap group may form its own subgroup within a wider IBS cohort, however this requires further investigation in larger number of patients. Ultimately, this data may enable more targeted treatment of IBS symptoms in hEDS versus IBS alone in the future.

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P0748

NEUROPSYCHOLOGICAL PROCESSES AT PLAY IN INSTRUMENTED BIOFEEDBACK FOR CHRONIC CONSTIPATION AND FERAL INCONTINENCE

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Introduction: While the clinical efficacy of anorectal biofeedback therapy (BF) as a treatment for constipation and faecal incontinence (FI) has been demonstrated [1], the psychological mechanisms through which it works are poorly understood. At its core, biofeedback engages patients in a learning process in which they learn to exert control over specific bodily functions. These learning processes involve both cognitive and emotional elements.

Aims & Methods: Given the uncertainty about the pathways through which these occur we sought a more detailed understanding of the psychological process that are altered during biofeedback which correlate with changes in patient perception of control and sensory function.

Patients referred to a specialist pelvic floor unit with either severe constipation or FI underwent 6 sessions of biofeedback after evaluation by a gastroenterologist. Clinical, physiological and psychological measurements were taken before, during and at the end of therapy. Changes in patient perception of bowel control and rectal sensation (first sensation of barostat balloon) were correlated with corresponding changes in neuropsychological, emotional measures.

Results: A total of 132 patients who met inclusion criteria were enrolled and completed biofeedback therapy during the study period. Of these, 78 had FI and 54 had constipation as their primary condition. Mean first sensation threshold increased by 7 points in FI and 4 in constipation from baselines of 47 and 46, respectively. Mean sense of control (10 point scale) increased by 2.7 in FI and 2.0 in constipation.

The strongest correlates of change in first sensation threshold for FI patients were emotion regulation (self $r = .32$, $p = .05$), treatment efficacy credibility ($r = .32$, $p = .05$), locus of control being chance ($r = .44$, $p = .007$) and generalised self-efficacy ($r = .42$, $p = .01$). Jointly these factors explained 33% of the variance. For constipation patients the strongest correlates were emotion regulation (positive $r = .41$, $p = .05$), executive function (global $r = -.52$, $p = .01$; metacognition $r = -.60$, $p = .002$; sm $r = -.41$, $p = .05$; wm $r = -.67$, $p = .0005$; tm $r = -.48$, $p = .02$), perceived stress (tension $r = .43$, $p = .04$), cognitive flexibility (total $r = .51$, $p = .01$; alternate $r = .48$, $p = .02$). Jointly these factors explained 60% of the variance.

In contrast, the strongest correlates of change in perceived control for FI patients were emotion regulation (acceptance $r = -.24$, $p = .04$; positive reappraisal $r = .24$, $p = .04$), treatment efficacy credibility ($r = .33$, $p = .005$), executive function (sh $r = -.28$, $p = .01$), perceived stress (joy $r = -.25$, $p = .03$). Jointly these factors explained 21% of the variance. For constipation patients the strongest correlations were with emotion regulation (acceptance $r = -.57$, $p < .001$; catastrophizing $r = .31$, $p = .01$), executive function (global $r = -.32$, $p = .03$; metacognition $r = -.35$, $p = .01$; pl $r = -.46$, $p = .0009$; tm $r = -.32$, $p = .02$), generalised self-efficacy ($r = -.36$, $p = .01$). Jointly these factors explained 37% of the variance.

Conclusion: Neuropsychological constructs appear to be more deeply involved in change in both patient perceived outcomes and rectal sensation in patients whose primary condition was constipation than those presenting with FI. Overall, change in both patient perception of control and their sensory function appear to be more strongly correlated with concomitant changes in psychological traits in constipation than FI. This may suggest constipation as a stronger target for investigation of psychological mechanisms of action in biofeedback.

References: 1. Enck P, Van der Voort IR, Klosterhalfen S. Biofeedback therapy in fecal incontinence and constipation. *Neurogastroenterology and motility* 2009; 21(11): 1133-41.

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P0749

TOWARDS A VISCERAL HYPERSENSITIVITY-ASSOCIATED MICROBIOME SIGNATURE: ANALYSIS OF A CLINICAL COHORT INDICATES, INDEPENDENT OF INTERVENTION, BASELINE DIFFERENCES AND COMPOSITIONAL SHIFTS RELATED TO VISCERAL SENSITIVITY CHANGES

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Introduction: The functional disorder Irritable Bowel Syndrome (IBS) is characterized by recurrent abdominal pain. Previously, an association between increased sensitivity to colonic stimuli (visceral hypersensitivity) and altered luminal gut microbes has been shown. To evaluate longitudinal changes of the microbiome associated with visceral sensitivity, we examined the microbiota of hypersensitive IBS patients who participated in a randomized control trial (Ludidi et al, 2014), aiming at decrease of visceral sensitivity through probiotics treatment.

No differences in visceral sensitivity were observed after probiotic treatment as compared to placebo, although visceral sensitivity decreased in a sub-set of patients.

Aims & Methods: We aimed to define a microbial signature associated with a decrease of visceral sensitivity, independent on the intervention. Sixteen hypersensitive Rome III IBS patients were selected for microbiome analysis (7 probiotics; 9 placebo), of which visceral sensitivity decreased in several patients after 6 weeks of treatment (3 vs. 5 respectively). Microbial DNA was isolated from frozen fecal sample scrapings, both at baseline and after treatment. DNA amplicons for bacteria-specific (16S) and fungi-specific (*Internal Transcribed Regions*, ITS-1) regions were sequenced. Microbial richness and compositional diversities were analyzed by employing linear mixed models (LME) and PERMANOVA on Bray-Curtis dissimilarity. Multilevel principal component analysis (PCA) was used to identify compositional shifts.

Results: Fungal diversity and composition could not be linked to improvement of visceral sensitivity. However, bacterial richness metrics are associated with the change from hypersensitive to normosensitive (FPD, linear mixed effect (LME); $p=0.017$; Observed species, $p=0.021$). Bacterial composition could not be related to visceral hypersensitivity while the multilevel PCA did show a compositional shift associated with a decrease of visceral sensitivity (MANOVA; $p=0.002$). This compositional shift was marked by a significant increase of *Akkermansia* (LME; $p=0.007$) in patients that had reduced visceral sensitivity.

Conclusion: Taken together, our initial analysis indicated that patient transition from hyper- to normosensitive phenotype associated with moderate diversity- and compositional changes of luminal bacteria. Low microbiome richness at baseline may be a predictor for improvement, independent of the intervention. The association between increased *Akkermansia* and reduced visceral sensitivity confirms earlier reports on inverse correlations of this mucus associated bacterium with abdominal pain. Future analyses will focus on differently abundant species or a consortium of microbes as predictors of decreasing of visceral sensitivity.

References: Ludidi et al., Neurogastroenterol Motil (2014)

Disclosure: Nothing to disclose

P0750

RECTAL HYPOSENSITIVITY: A COMMON PATHOPHYSIOLOGICAL FINDING IN PATIENTS WITH HYPERMOBILE EHLERS-DANLOS SYNDROME

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Introduction: Hypermobile Ehlers-Danlos syndrome (hEDS) is a multisystemic disorder associated with multiple comorbidities, including functional somatic syndromes. Though several studies have confirmed a high prevalence of GI symptoms, particularly constipation, in hEDS (Nelson et al., 2015, Zarate et al., 2010, Mohammed et al., 2010), these studies are limited by small sample sizes, a paucity of data on anorectal physiological testing, and absence of control groups. Consequently, it is unclear which pathophysiological processes may be contributing to constipation in hEDS patients, and whether any of them are over-represented compared to constipated individuals without hEDS.

Aims & Methods: To evaluate symptom presentation and underlying pathophysiology of anorectal dysfunction in consecutive hEDS patients with functional constipation.

Retrospective case-control study of patients presenting to a tertiary GI Physiology Unit for investigation of functional constipation. 73 consecutive female patients with an established diagnosis of hEDS, meeting Rome IV criteria for functional constipation, were age matched (± 5 years) to 146 consecutive female controls (1:2 ratio). Patients were considered for enrolment in the control group provided they scored 0 in the joint hypermobility validated 5-point screening questionnaire (Hakim and Grahame, 2003) and also met the Rome IV core criteria for functional constipation. Demographics, specific symptoms and results of comprehensive lower GI physiology testing (including rectal sensation to balloon distension, whole gut transit studies and defaecography) were compared between hEDS patients and controls.

Results: (Table 1): The hEDS group had significantly fewer parous females compared to controls (41.1% vs. 70.6%; $p = 0.001$), and were more likely to report a long duration of constipation (≥ 5 years: 78.1% vs 60.3%, $p = 0.009$). hEDS patients more often had a score of ≥ 12 on the Cleveland Clinic constipation score compared to controls (97.3% vs. 87.7%; $p = 0.020$). On diagnostic testing, hEDS patients were three times more likely to have rectal hyposensitivity compared to controls (32.4% vs 11.0%; $p = 0.0001$). There were no significant differences in the prevalence of delayed gut transit, or functional or structural rectal morphological abnormalities on defaecography between the two groups. (Table 1).

	hEDS (%) n = 73	No hEDS (%) n = 146	p value
Duration of constipation in years (≥ 5 years)	57 (78.1)	88 (60.3)	0.009
Results of diagnostic testing			
Rectal hyposensitivity on sensory testing	23 (32.4)	16 (11.0)	0.0001
Functional abnormalities on defaecography	32 (46.4)	51 (34.9)	0.108
Structural abnormalities on defaecography	45 (65.2)	89 (61.0)	0.548
Delayed gut transit on radio-opaque marker study	19 (36.5)	37 (41.6)	0.555

[Table 1. Demographics, symptoms of constipation and anorectal physiological investigations in hEDS patients vs controls]

Conclusion: Rectal hyposensitivity was diagnosed in 32.4% of hEDS patients with functional constipation and was three times more common compared to non-hypermobile controls with functional constipation. The cause of rectal hyposensitivity in hEDS patients is unclear, but may be due to altered rectal biomechanics (e.g. hypercompliance), a 'true' sensory neuropathy, or both. Further studies are needed to explore this.

Disclosure: Nothing to disclose

P0751

ASSESSMENT OF ASCENDING COLONIC DISTENSION FOLLOWING INTRAGASTRIC ADMINISTRATION OF FRUCTANS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME VERSUS HEALTHY CONTROLS: A DOUBLE-BLIND RANDOMISED CONTROL TRIAL COMBINING GASTROINTESTINAL AND BRAIN IMAGING

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Introduction: Gastrointestinal magnetic resonance imaging (GI MRI) has shown that following FODMAP ingestion, hypersensitivity to colonic distension - rather than excessive gas volume - explains irritable bowel syndrome (IBS) symptoms when compared to healthy controls (HC) [1].

Aims & Methods: The aim of this study was to assess the effect of FODMAP ingestion on distension and gas volumes in the ascending colon (AC) while also recording brain responses in a neuroimaging paradigm. Female IBS patients & healthy controls (HC) underwent GI MRI before, 1- & 2- hours after intragastric infusion of 500 ml fructans (40g), glucose (40g) or saline in a randomized double-blind design; functional magnetic resonance imaging of the brain was performed from 10 minutes before until 50 minutes after infusion. All participants followed a low-FODMAP diet 24h and overnight fast before each scan. AC volumes and gas were segmented using region of interest tools (Horos®, Annapolis, MD USA) on T2-weighted coronal images. Volumetric calculations were performed in MATLAB (2019a, Mathworks) and linear mixed model analysis using PROC_MIXED (SAS Institute Inc).

Results: 13 IBS patients (age: 27 ± 7 yrs; BMI: 24.0 ± 4.20) and 13 HC (age: 31 ± 12 yrs; BMI: 22.3 ± 1.75) participated. IBS patients were younger (p=0.018) and had higher BMI (p<0.001) compared to HC. Baseline AC volumes were 334cm³ (IQR: 273 to 401) in IBS and 393cm³ (IQR: 319 to 448) in HC and intraclass correlation coefficient (ICC) was 0.72 (95% CI: 0.54 to 0.85). After controlling for age, BMI and visit there were no differences in baseline AC volume between IBS and HC (p = 0.19). Baseline AC gas was 9cm³ (IQR: 6 to 15) in IBS and 8cm³ (IQR: 4 to 18) in HC and ICC was 0.10 (95% CI: -0.12 to 0.37).

Two hours after fructans infusion, AC volumes increased by 247cm³ (IQR: 151 to 324) in IBS and 303cm³ (IQR: 169 to 420) in HC. AC gas increased by a median of 35cm³ (IQR: 29 to 99) in IBS and 122cm³ (IQR: 31 to 229) in HC. Maximal change (Δ) in AC volume after glucose was lower and observed at 1hr in IBS: 48cm³ (IQR: 25 to 96) compared to at 2hr in HC: 21cm³ (IQR: -34 to 34). After controlling for age, BMI, visit, time and baseline volumes; there was a strong main effect of condition (fructans, glucose or saline) on both AC volume and gas (p<0.0001). Differences in AC gas volume over time were observed with a trend for IBS patients' gas to increase at 1-hr post-infusion (p = 0.09) with no further increase by 2-hrs (p = 0.48). In contrast, HC gas volumes increased from 1- and 2 hrs (p = 0.01) and there was a patient-by-time interaction, independent of the nutrient infused (p = 0.02).

Conclusion: Under controlled experimental conditions, good consistency was observed in baseline AC volumes but intra-individual variation in baseline gas was high. Intra-gastric infusion of fructans led to a pronounced increase in AC volume and gas in both groups compared to glucose and saline. This is consistent with the previous work by Major et al [1]. The heterogeneity of GI parameters at baseline and in response to intra-gastric administration of specific nutrients suggests that GI MRI could complement brain imaging in the investigation interoceptive processing. Previous analysis of the pain responses in these participants found differential activation patterns in pain-responsive brain regions in IBS compared to HC following fructans versus glucose and saline [2]. Future work will combine GI and brain responses with subjective symptoms and gut peptides to fully characterise gut-brain interactions in health and disease.

References: [1] Major, G. et al. Colon Hypersensitivity to Distension, Rather Than Excessive Gas Production, Produces Carbohydrate-Related Symptoms in Individuals With Irritable Bowel Syndrome. *Gastroenterology* 152, 124-133 e122, doi:10.1053/j.gastro.2016.09.062 (2017). [2] Masuy et al. Increased symptom and brain responses to intra-gastric administration of FODMAPs in patients with irritable bowel syndrome vs healthy subjects. 32 (S1) Special Issue: FNM 2020 - 4th Meeting of the Federation of Neurogastroenterology and Motility, 25 - 28 March 2020, Adelaide Convention Centre, Adelaide, Australia <https://doi.org/10.1111/nmo.13816>

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P0752

CONCENTRATION OF SEROTONIN AND THEIR METABOLITES IN COLONIC MUCOSA IN PATIENTS WITH DIVERTICULOSIS, FUNCTIONAL BOWEL DISORDERS AND HEALTHY CONTROLS

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Introduction: Functional bowel disorders (FBD) and diverticulosis are widespread in general population. Their pathogenesis is very complex and still not fully understood. Serotonin (5-HT) was established as an important modulator of bowel motility. Drugs affecting serotonergic system are successfully used in Europe and US. However, number of studies that tried to evaluate a concentration of serotonin in serum and mucosa in patients with gastrointestinal disorders have shown different and sometimes opposite results.

Aims & Methods: The aim of the study was to evaluate the concentration of catecholamines, serotonin and its metabolite- 5-HIAA in the colonic mucosa. Mucosal samples of ascending (right side, R) and descending (left side, L) colon were taken from 85 patients (35 males and 50 females) who underwent colonoscopy in The Department of Gastroenterology and Internal Medicine of Medical University of Warsaw, Poland. According to results of the endoscopic procedure and symptoms evaluated by ROME IV Diagnostic Questionnaire individuals were assigned to 4 groups: healthy controls (n=28; M=11, F=17), diverticulosis (n=37; M=18, F=19), functional diarrhoea (n=14; M=5, F=9) and functional constipation (n=6; M=1, F=5). Ten patients also met IV ROME Irritable Bowel Syndrome (IBS) criteria. Concentration of the serotonin and its' metabolite, 5-hydroxyindoleacetic acid (5-HIAA), was measured using high-performance liquid chromatography. Colonic transit time (CTT) was evaluated with SITZMARKS capsule.

Results: In healthy controls both median difference of 5HT (L: 10369 vs R: 8307 pg/mg, p<0.001) and 5-HIAA (L: 3761 vs R: 3158, p<0.005) level in tissue obtained from the left side of the colon was higher than from the right

side. In patients with diverticulosis difference in 5HT (L: 10874 vs P:6395 pg/mg, $p < 0.001$) but not in 5-HIAA concentration was found (L: 3507 vs R: 3395 pg/mg, $p = 0.11$). The value of 5-HIAA/5-HT ratio was also lower in the descending colon ($p = 0.018$). On the contrary, in group with diarrhoea significant differences in 5-HIAA (L: 4701 vs 3359 pg/mg, $p = 0.035$) but not in 5-HT (L: 9058 vs R: 8144 pg/mg, $p = 0.715$) level were obtained. There were no differences in median concentration of 5HT and 5HIAA between tested groups. Patients in diverticulosis group were significantly older than in a control group (52.0 vs 69.0 yo, $p < 0.001$). In tested groups we did not find significant correlation between CTT and mucosal concentration of 5HT nor 5HIAA.

Conclusion: Bioavailability and metabolism of serotonin vary between ascending and descending colon in FBD and diverticulosis. Results of our study suggest that 5HIAA/5HT ratio rather than isolated 5HT or 5HIAA tests is a better tool to evaluate serotonin-induced changes of the bowel functions.

Disclosure: Nothing to disclose

P0753 WITHDRAWN

P0754 WITHDRAWN

P0755

REGION SPECIFIC EFFECT OF STW 5 ON MURINE COLON MOTILITY

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Introduction: Colonic dysmotility is a hallmark pathophysiology in many functional and organic bowel disorders that affect the quality of life. STW 5 is an herbal medicinal product with a proven clinical efficacy in functional gastrointestinal disorders including functional dyspepsia and irritable bowel syndrome (IBS).

Aims & Methods: This study aims to evaluate the effect of STW 5 on colonic motility and to analyze its region specific effects on the proximal and distal parts of the murine colon. An *ex vivo* luminal perfusion setup has been used to investigate the impact of STW 5 on the healthy murine gut. Recorded motility patterns during perfusion were analyzed by mean interval value, number of contractions, and alterations of gut diameter that converted into a heatmap. Velocity studies have been used to evaluate motility responses to STW 5 depending on colonic region.

Results: Exposure of murine colon to STW 5 resulted in an activation of colonic motility associated with a reduction in mean interval and a decrease in the gut diameter. Velocity studies revealed a decrease in distal motility in comparison to the proximal part of the murine colon, which suggests a relaxing rather than tonicizing effect of STW 5 on the distal part.

Conclusion: Our findings confirm the functional impact of STW 5 on colon motility and support its proven clinical efficacy in bowel disorders such as IBS and constipation.

Disclosure: This study was funded by Bayer Consumer health, Darmstadt, Germany.

P0756

ROLE OF β -ARRESTIN 2 IN OPIOID-INDUCED CONSTIPATION

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Introduction: The chronic use of opioids generally achieves effective pain control although with the onset of various side effects, including gastrointestinal (GI) dysfunction.¹ Opioid-induced constipation (OIC) is frequent and worsens the quality of life of patients chronically treated with opioids for cancer (51-87%) and non-cancer pain (41-57%).² Mu-opioid receptor (MOR) activation by opioids evokes β -arrestin 2 signalling involved in side effect mechanisms, whereas G-protein signalling triggers analgesia.³ Morphine treatment in β -arrestin 2 knockout mice results in greater and prolonged analgesia, with a milder constipation and respiratory depression compared to wild types.^{4,5} However, recent studies challenged these previous results showing that the failed β -arrestin 2 recruitment at MOR and the loss of its expression did not ameliorate morphine- or fentanyl-induced constipation, although analgesia improved.^{6,7}

Aims & Methods: This study aims to clarify the contribution of the β -arrestin 2 in therapeutic and adverse effect elicited by opioid drugs, focusing on OIC. Data are directed to better understand whether G-protein-biased MOR agonists may represent a safer pain-control therapy than canonical opioids. Methods: β -arrestin 2 knockout (*Arrb2^{-/-}*) and wild type C57 BL/6J (*Arrb2^{+/+}*) mice were compared. Opioids were intraperitoneally injected (10ml/kg volume/ body weight). Analgesic effect of opioids was evaluated with the tail withdrawal test. Cumulative dose-response curves were performed and ED50 calculated and compared among treatments and genotypes. Morphine was tested at 1, 3, 10 mg/kg and fentanyl at 0.1, 0.3, 1 mg/kg doses. At same doses, whole GI transit was assessed in the 6 hours after single opioid injection, via *faecal boli* accumulation assay. Weight and number of stools were recorded and constipating ED50 calculated at the endpoint. Water content of total *faecal pellet* collected was estimated. Colonic transit delay was evaluated by bead expulsion test and compared among *Arrb2^{-/-}* and *Arrb2^{+/+}* treated with equianalgesic doses of opioids.

Results: Untreated *Arrb2^{-/-}* and *Arrb2^{+/+}* mice showed comparable analgesic thresholds and GI transit. Analgesic ED50 of morphine and fentanyl is 2-fold lower in *Arrb2^{-/-}* vs. *Arrb2^{+/+}* mice. Constipating ED50 of morphine is 2-fold greater in *Arrb2^{-/-}* vs. *Arrb2^{+/+}*, while fentanyl showed same potency in both genotypes. Water content in stools is significantly decreased only in *Arrb2^{+/+}* mice treated with morphine 10 mg/kg (20±7%) compared to vehicle (49±2%; $P < 0.05$). Upon equianalgesic doses of opioids, colonic transit of *Arrb2^{-/-}* mice is significantly less delayed (morphine 161±11 min; fentanyl 200±24 min) than in *Arrb2^{+/+}* mice (morphine 285±31 min; fentanyl 364±55 min, $P < 0.05$).

Conclusion: Our data confirmed that β -arrestin 2 plays a critical role in regulating MOR mediated effects elicited by canonical opioids. Specifically, acute treatment with opioids exhibited greater analgesic effects in *Arrb2^{-/-}* vs. *Arrb2^{+/+}* mice, with less OIC in equianalgesic conditions. Morphine and fentanyl exhibit the highest therapeutic index in *Arrb2^{-/-}* vs. *Arrb2^{+/+}* mice.

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Disclosure: Nothing to disclose

P0757 WITHDRAWN

P0758

AFTER 25 YEARS AS A EUROPEAN LAXATIVE POLYETHYLENE GLYCOL HAS MORE SCIENTIFIC PUBLICATIONS AND A FASTER-GROWING CLINICAL EVIDENCE BASE THAN OTHER COMMON TREATMENTS FOR CONSTIPATION OR FAECAL IMPACTION

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Introduction: In 2020, polyethylene glycol (PEG) has been available in Europe as a laxative for 25 years. To characterize its general importance in medicine and specific importance in constipation or faecal impaction (FI), including 21st century trends, we performed a bibliometric analysis of the published literature on PEG versus other common laxatives and versus salicylic acid, a classic medicine with enduring presence in the medical literature.

Aims & Methods: PubMed was researched for publications until 1 January 2020, for four commonly used laxatives. General medical importance was assessed as the total publications volume per substance. Search terms were for PEG "polyethylene glycol OR macrogol OR PEG3350 OR PEG4000", for lactulose "lactulose OR 4-O- β -D-Galactosyl-D-fructose", for picosulfate "picosulfate OR picosulphate", and for prucalopride "prucalopride". For salicylic acid, the terms "aspirin OR salicylic acid", were used. The specific importance in constipation or FI was assessed per laxative, first by using a refined search with the added terms "AND (constipation OR faecal impaction OR faecal impaction)", together with a filter for either "clinical trials" or "randomized clinical trials" (RCT). The 21st century trends were assessed as 5-year means with standard errors of the mean (SE) of annual published clinical trials per laxative in 2001-2019 (last period 4 years). Results were compared using the 1-sided t-test versus PEG and using linear regression trends of the actual annual volumes.

Results: PEG had more publications than any other laxative (83 827 vs lactulose 3 891, picosulfate 339, or prucalopride 369) or even salicylic acid (83 827 vs 80 301) (Table 1). In constipation or FI, PEG had more published clinical trials overall and more RCT than lactulose, picosulfate or prucalopride (all trials: 136 vs 109, 10, or 35; and RCT: 111 vs 85, 9, or 30). In each period from 2001 to 2015, more clinical trials in constipation or FI were published on PEG versus picosulfate or prucalopride ($P < 0.018$ for all comparisons). The mean annual volume of clinical trials on PEG exceeded that of lactulose in 2011-2015 (6.2 ± 0.7 vs 3.8 ± 0.7 ; $P = 0.025$) and in 2016-2019 (9.0 ± 1.7 vs 4.3 ± 0.9 ; $P = 0.025$). Similarly, in 2016-2019, trials on PEG

also outnumbered those on picosulfate (9.0 ± 1.7 vs 0.3 ± 0.3 ; $P = 0.003$) or prucalopride (9.0 ± 1.7 vs 1.8 ± 0.6 ; $P = 0.004$). With an average annual increment of 0.265 new trials per year [95% CI: 0.037-0.493], the linear regression analysis showed that PEG was the only laxative to demonstrate a statistically significant positive annual growth trend of published new clinical trials in the 21st century.

	PEG	Lactulose	Picosulfate	Prucalopride	Salicylic acid
Total number of publications by 1 Jan 2020	83827	3891	339	369	80301
Total published clinical trials	4359	704	102	46	8157
Evidence base 1 Jan 2020: All clinical trials in constipation or FI	136	109	10	35	NR
High-quality evidence base 1 Jan 2020: Randomized controlled trials in constipation or FI	111	85	9	30	NR
Evidence base growth (2001-2005): All clinical trials in constipation or FI, annual mean $\pm$ SE; P vs PEG	3.6 ± 0.4 ; $P = 0.5$	2.6 ± 1.1 ; $P = 0.205$	0.0 ± 0.0 ; $P < 0.001$	1.0 ± 0.5 ; $P = 0.002$	NR
Evidence base growth (2006-2010): All clinical trials in constipation or FI, annual mean $\pm$ SE; P vs PEG	6.0 ± 1.4 ; $P = 0.5$	3.6 ± 1.0 ; $P = 0.100$	0.6 ± 0.4 ; $P = 0.003$	1.8 ± 0.9 ; $P = 0.017$	NR
Evidence base growth FI (2011-2015): All clinical trials in constipation or, annual mean $\pm$ SE; P vs PEG	6.2 ± 0.7 ; $P = 0.5$	3.8 ± 0.7 ; $P = 0.025$	0.6 ± 0.2 ; $P < 0.001$	2.4 ± 0.8 ; $P = 0.004$	NR
Evidence base growth (2016-2019): All clinical trials in constipation or FI, annual mean $\pm$ SE; P vs PEG	9.0 ± 1.7 ; $P = 0.5$	4.3 ± 0.9 ; $P = 0.025$	0.3 ± 0.3 ; $P = 0.001$	1.8 ± 0.6 ; $P = 0.004$	NR
21st century evidence base growth trend, annual increment [95% CI]	0.265 [0.037,0.493]	0.105 [-0.067,0.277]	0.018 [-0.036,0.071]	0.086 [-0.052,0.224]	NR

[Table 1. Scientific publications in Pub Med, on PEG versus other commonly used laxatives or salicylic acid. NR = Not relevant. FI = Faecal Impaction.]

Conclusion: PEG is the most published commonly used laxative substance, a molecule so common in contemporary medicine that it now has more publications than even aspirin. The wide usage across many medical areas makes PEG uniquely well characterised compared to other laxatives. Among laxatives, PEG has the largest number of randomized controlled trials in constipation or FI and PEG also has the largest mean annual growth volume of its evidence base.

Disclosure: JH, OH and BA are employees of Norgine Ltd.

P0759

REAL-WORLD DATA ON UTILISATION AND SAFETY OF POLYETHYLENE GLYCOL 3350 WITH ELECTROLYTES IN CHILDREN UNDER 2 YEARS FOR THE TREATMENT OF CONSTIPATION

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Introduction: Polyethylene glycol 3350 with electrolytes (PEG 3350+E) is licensed for constipation in children aged 2 years and over in many countries. This study investigated real-world use (off label) in children < 2 years of age in the UK.

Aims & Methods: Our primary objective was to examine utilisation and safety of PEG 3350+E for treatment of constipation in this age group. The secondary objective was to assess the impact of confounding by indication, posology and duration of treatment on incident events (IEs) identified.

This retrospective cohort study with a PEG 3350+E exposed cohort used the Clinical Research Practice Datalink (CPRD) GOLD database. Patients (pts) who were first prescribed PEG 3350+E under 2 years of age for the treatment of constipation between 2003 and 2019 were included. CPRD GOLD contains routine-clinical data for over 800 UK primary care practices. Reasons for clinical consultations on treatment were used to identify and quantify IEs. Clinical consultations prior to starting the medication described pts medical history. Treatment utilisation was quantified as treatment episodes (TE) and prescribed total daily dose (TDD). Demographic, drug utilisation and safety information variables were also obtained.

Results: A total of 13235 pts prescribed PEG 3350+E for constipation were identified. 9380 pts (70.9%) were aged between 12 and < 24 months when first prescribed PEG 3350+E with a median age of 1.2 years (IQR 0.9,1.6) at first TE. The majority of the pts (68.4%) had one TE and 10.7% had at least three TEs. The mean duration of continuous exposure, in the first TE, was 88.9 days (range 60.0-691.0). The prescribed TDD was 1 to 2 sachets in 99.7% of pts (where specified). The most commonly prescribed TDD was 1 sachet (60.1%) and mean TDD varied across TEs and age groups. Other osmotic laxatives were prescribed as prior medication in 39.1% and stimulant laxatives in 7.1% of reported medications. Constipation and related symptoms, was the most commonly reported IE on treatment (n=3340;25.2%). The incidence of diarrhoea (3.0%), vomiting (4.1%) and abdominal pain (0.5%) was low and consistent with the product label. Among IEs that could be potentially related to electrolyte disturbance (2.0% pts), the most commonly reported was fatigue. General patterns of IEs on treatment remained the same after stratifying by TDD at index and TE duration. Only 1.2% of pts had reported constipation and related symptoms within the 30 days after stopping the first TE, suggesting improvement in symptoms.

Conclusion: Our study provides the largest real-world data on the utilisation and safety of PEG 3350+E in children < 2 years of age. It demonstrates that PEG 3350+E has been widely prescribed for the treatment of constipation in this age group whilst not yet licensed for use. The most commonly prescribed TDD was the same as the recommended starting dose for pts aged 2 to 6 years. The most common IEs identified were indication-related with no new safety concerns identified in this age group. The low

incidence of constipation after stopping treatment suggests good control of symptoms. These data provide real-world evidence on the use of PEG 3350+E in children < 2 years of age for the treatment of constipation.

Disclosure: The Drug Safety Research Unit (DSRU) is an independent academic institution, which works in association with the University of Portsmouth. It receives unconditional donations from pharmaceutical companies. The DSRU has received funds from Norgine, the marketing authorisation holder for Movicol paediatric plain (Polyethylene glycol 3350 with electrolytes), to conduct this study. The DSRU has the final decision regarding the publication of papers or abstracts and their content. Dr Debabrata Roy and Professor Saad Shakir have no other conflicts of interest to declare. Dr Bharat Amlani and Dr Fatma Akriche are employees of Norgine. Dr Petter Malmberg has provided medical consultancy and advisory services in the preparation of an application to extend Movicol (Polyethylene glycol 3350 with electrolytes) age group license and has for this service received payment from Norgine. Dr Petter Malmberg is affiliated with the: 1) Unit of Pediatric Gastroenterology and Nutrition, Sachs' Children and Youth Hospital, Stockholm, Sweden, 2) Division of Clinical Epidemiology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden and the 3) Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden.

P0760

CLASSIFYING PATHOPHYSIOLOGICAL CONDITIONS OF CONSTIPATION USING ABDOMINAL ULTRASONOGRAPHY

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Introduction: Chronic constipation is a common gastrointestinal disorder which widely affects patients' quality of lives with additional health care and costs. Constipations could be classified into 3 subgroups, rectal evacuation disorders, slow-transit constipation, or normal-transit constipation. Because each group requires different treatment options, specialized examinations are needed to classify them. According to the previous study, rectal evacuation disorders containing greater volume of rectal gas can be visualized by X-ray. Moreover, we have previously reported that abdominal ultrasonography, as comparison with computerized tomography, could also diagnose stool distribution and form.

Aims & Methods: The aim of this study was to classify constipation into 3 pathophysiological conditions using abdominal ultrasonography and X-ray. 85 constipated patients who visited our constipation outpatient clinic between May 2019 and January 2020 were enrolled. We also enrolled 10 non-constipated patients as control subjects. We asked constipated patients to fill out Constipation Scoring System (CSS) and Japanese version of the Patient Assessment of Constipation Quality of Life questionnaire (JPAC-QOL) scores at their first visit. We performed abdominal ultrasonography and X-ray on them and identified stool distribution to ascending colon (A), transvers colon (T), descending colon (D), sigmoid colon (S), and rectum (R) using abdominal ultrasonography. We examined rectal gas by X-ray and defined that patients with rectal gas as rectal evacuation disorders, patients without rectal gas and fulfilled with stool toward S and/or R as slow-transit constipation, and patients without rectal gas but no stool in both S and R as normal-transit constipation.

Results: Among non-constipated patients, stool was not observed on the anal side of D after defecation but was observed toward S before defecation. However, stool was never observed in the rectum. The total number

of constipated patients were 85 (male 27, female 58) and the average age was 64 ± 19 years old. The abdominal ultrasonography and X-ray classified constipation patients into 3 groups, 22.4% in the rectal evacuation disorders group, 55.2% in the slow-transit constipation group, 22.4 % in the normal-transit constipation group, without adverse event. Although 52.6% in the rectal evacuation disorders group and 57.5% in the slow-transit constipation group represented hard stool (Bristol Stool Form Scale (BSFS) 1-2), 68.4% represented normal form stool (BSFS 3-5) in the normal-transit constipation group. All constipation patient group had mainly complained about stool remaining even after defecation, and according to CSS, the proportion of each group was 68.4%, 78.7%, and 84.2%, respectively. Among 28 repeat-tested constipation patients, all patients resulted in normal stool form (BSFS 3-5) and 92.9% of the patients improved JPAC-QOL scores after constipation treatment.

However, symptoms improvement was not reflected in pathophysiological examination by abdominal ultrasonography even after their symptom improved.

Conclusion: The abdominal ultrasonography and X-ray successfully classified pathophysiological condition in constipated patients. Pathophysiological change was not shown before and after satisfied constipation treatment compared to symptom improvement.

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Disclosure: Nothing to disclose

P0761

CLINICAL CHARACTERISTICS, ANAL SPHINCTER PRESSURE AND RECTAL SENSATIONS IN VIETNAMESE PATIENTS WITH DYSSYNERGIC DEFECATION ON HIGH-RESOLUTION ANORECTAL MANOMETRY

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Introduction: Dyssynergic defecation (DD) is a condition due to the inability to coordinate the abdominal and pelvic floor muscles in passing stool. High-resolution anorectal manometry (HRAM) is essential for a diagnosis of DD with patterns of inadequate pushing force, paradoxical anal sphincter contraction and impaired anal sphincter relaxation. However, HRAM is a new technique in Vietnam with limited data, especially for dyssynergic defecation patients.

Aims & Methods: The study was conducted to evaluate clinical symptoms, anal sphincter pressure and rectal sensations in patients with DD on HRAM. This is a retrospective study on patients who were ≥ 18 years old and diagnosed with DD on HRAM. HRAM was performed with a water-perfused 20-channel catheter in the Solar GI system. We excluded patients with Hirschsprung disease, anorectal masses, polyps, fissures or fistulas, active hemorrhage, severe internal hemorrhoids, external hemorrhoids or complicated hemorrhoids, or patients with impaired hearing or mental disorders. Dyssynergic defecation was classified into four types based on Rao's classification.

Results: From July 2018 to July 2019, 81 patients were recruited. The female-to-male ratio was 1.5, the mean age was 47.4 ± 14.3 . 48.1% of the patients had symptoms related to bowel habit changes (constipation and

diarrhea). On HRAM, the mean anal canal length, mean anal resting pressure, mean anal squeeze pressure, and mean anal endurance pressure were 2.77 ± 0.47 cm, 67.65 ± 22.03 , 150.07 ± 47.9 , and 138.8 ± 48.9 (mmHg), respectively and were significantly higher in males. In the rectal sensation test, the median first sensation, urging defecation, and maximum tolerable volume were 30, 85 and 140 mmHg, respectively. In the push maneuver, dyssynergic defecation type I was the most common (48 patients), followed by type II (16), type III (16), and type IV (1). There were no differences among 4 types in anal canal length, anal squeeze and endurance pressures, and rectal sensations.

Conclusion: Bowel habit changes are common in Vietnamese DD patients. The most common type of DD is type I and there is no differences in anal canal pressures and rectal sensations among 4 types.

Disclosure: Nothing to disclose

P0762

DIAGNOSTIC AND THERAPEUTIC APPROACH TO CHRONIC CONSTIPATION: A NATIONWIDE MEDICAL SURVEY

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Introduction: Chronic constipation is a prevalent condition. In Portugal there are no local guidelines and there is no data regarding its diagnostic and therapeutic approach in clinical practice.

Aims & Methods: This study aims to characterize the management of chronic constipation by colorectal surgeons and gastroenterologists dedicated to Coloproctology.

A digital invitation to fill out a questionnaire regarding the management of chronic constipation was sent to the physicians of the Portuguese Society of Coloproctology that gathers most of the clinicians dedicated to coloproctology in Portugal. The questionnaire included demographic data and 13 questions regarding their clinical practice - clinical history, physical examination, clinical maneuvers and evaluation scales, complementary diagnostic tests, and pharmacological and non-pharmacological therapeutic options.

Results: Fifty-seven physicians answered the survey, 25 (43.9%) gastroenterologists and 32 (56.1%) colorectal surgeons. Regarding anamnesis of patients with constipation, gastroenterologists question more about physical activity ($\phi = -0.351$), ingestion of liquids ($\phi = -0.311$) and sexual abuse history ($\phi = -0.316$) while surgeons ask more about digital maneuvers to defecate ($\phi = 0.343$) and use more the Cleveland constipation scoring system ($\phi = 0.393$). In physical examination, surgeons perform a more extensive evaluation in their clinical practice ($r = -0.603$), perform more the bimanual rectal and vaginal exam ($\phi = 0.498$), Valsalva maneuver ($\phi = 0.516$), gynecological exam ($\phi = 0.388$) and rectal digital examination ($\phi = 0.315$).

Concerning diagnostic tests, surgeons prescribe more often anorectal manometry ($\phi = 0.392$), colonic transit time ($\phi = 0.531$), conventional and magnetic resonance defecography ($\phi = 0.563$) and radiological exams ($\phi = 0.464$). Regarding treatment, gastroenterologists prescribe more often drug combinations ($\phi = -0.355$) while surgeons prescribe more biofeedback ($\phi = 0.439$) and colectomy ($\phi = 0.540$).

Physicians with more than 10 years of experience use less the Bristol Stool Form Scale ($\phi = -0.330$) and report more frequently to use no clinical scales ($\phi = 0.267$). Clinicians with less than 10 years of experience prescribe more often biofeedback ($\phi = -0.267$).

Conclusion: There are differences in the diagnostic and therapeutic approach of chronic constipation depending on the area of medical specialty (Gastroenterology/General Surgery) of Coloproctology. The extent of clinical experience seems to impact less the approach.

Disclosure: Nothing to disclose

P0763

EFFICACY AND TOLERABILITY OF STIMULANT LAXATIVES IN ELDERLY - RESULTS OF A POST-HOC ANALYSIS OF TWO RANDOMIZED CONTROLLED CLINICAL TRIALS WITH BISACODYL/SODIUM PICOSULFATE

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Introduction: Chronic functional constipation increases with advancing age (particularly > 65 years) [1]. Bisacodyl (BIS) and sodium picosulfate (SPS) are well-established, guideline recommended treatment options [2]. Notably, there is no in-depth analysis available yet comparing the efficacy and safety of stimulant laxatives in an elderly vs. younger population.

Aims & Methods: A post-hoc analysis was performed to explore whether efficacy and tolerability of a stimulant laxative treatment differs in patients with chronic constipation ≤ 65 years of age versus patients > 65 years of age, hereby defined as elderly.

Results of two recent clinical trials (BIS: EudraCT No. 2007-001991-34 [3]; SPS: EudraCT No. 2007- 002087-10 [4]) were analysed in view of the primary endpoint (adjusted mean difference over placebo in weekly complete spontaneous bowel movements (wCSBM, week 1-4) and the respective secondary endpoint (weekly spontaneous bowel movements (wSBM, week 1-4)). Further, safety parameters in view of reported (Serious) Adverse Events ((S)AEs) were analysed.

Results: Over the four weeks of treatment both, BIS and SPS, showed statistically significant improvement over placebo in the number of weekly bowel movements in both age groups (wCSBM [week 1-4] (all groups): $p < 0.01$, wSBM [week 1-4] (all groups): $p < 0.001$).

Interestingly, patients ≤ 65 years treated with BIS showed a higher stool frequency over placebo compared to the elderly population (wCSBM [week 1-4]: 3.8 (±0.47) / 2.2 (±0.55) (≤ 65 years / > 65 years); wSBM [week 1-4]: 5.3 (±0.56) / 3.8 (±0.68); respectively), whereas, in the SPS study the stool frequency was higher in the elder compared to the younger population (wCSBM [week 1-4]: 2.0 (±0.73) / 1.8 (±0.32) (> 65 years / ≤ 65 years); wSBM [week 1-4]: 4.0 (±1.04) / 3.2 (±0.38); respectively).

There was a similar reporting rate of total AEs in patients ≤ 65 years vs. elderly in both trials (BIS: 67.9% vs. 74.3% and SPS: 40.6% vs. 48.1%, for more information see Table). Amongst these the primary system organ class (SOC) 'gastrointestinal disorders' was the most prevalent. A tendency for a slightly higher proportion of diarrhoea but lower proportion of abdominal pain could be observed in the older age group in both trials (Table). No Fatal cases occurred and reported SAEs were non-related to study medication.

Investigator-defined drug-related AEs decreased from 63.5% / 53.9% in week 1 to 7.0% / 4.2% (> 65 years / ≤ 65 years) in week 2 in the BIS study and from 38.9% / 28.6% to 3.7% / 4.0% (> 65 years / ≤ 65 years) in the SPS clinical trial. The decrease was presumably due to individual dose-adjustments.

	Placebo		Bisacodyl		Placebo		Sodium Picosulfate	
	≤ 65 yrs	> 65 yrs	≤ 65 yrs	> 65 yrs	≤ 65 yrs	> 65 yrs	≤ 65 yrs	> 65 yrs
	N (%) affected	N (%) affected	N (%) affected	N (%) affected	N (%) affected	N (%) affected	N (%) affected	N (%) affected
Number of patients	82	35	165	74	100	33	175	54
Total with AEs	32 (39%)	7 (20%)	112 (67.9%)	55 (74.3%)	18 (18%)	5 (15.2%)	71 (40.6%)	26 (48.1%)
Gastrointestinal disorders (SOC)	13 (15.9%)	2 (5.7%)	101 (61.2%)	49 (66.2%)	10 (10%)	2 (6.1%)	63 (36%)	24 (44.4%)
Abdominal pain	2 (2.4%)	1 (2.9%)	43 (26.1%)	11 (14.9%)	2 (2%)	1 (3%)	9 (5.1%)	1 (1.9%)
Abdominal pain upper	2 (2.4%)	1 (2.9%)	14 (8.5%)	3 (4.1%)	nr	nr	3 (1.7%)	nr
Diarrhea	nr	nr	75 (45.5%)	44 (59.5%)	5 (5%)	1 (3%)	50 (28.6%)	21 (38.9%)

[Table: Prevalence of AEs per treatment group and age cluster. Overview of AEs with a frequency of >5% in any treatment group (nr=not reported)]

Conclusion: Stimulant laxatives are effective and well tolerable in both, the older and younger patient population. Reporting rates for AEs were similar in both age groups. Overall, BIS and SPS are effective in chronic constipated patients > 65 years, the safety profile in this age population reflects the well-established safety profile for stimulant laxative with a slight tendency for higher rates of diarrhea and less sensations of abdominal pain.

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P0764

THE EFFECT OF PARENTS' MORBIDITY STATUS ON CHILDREN'S ABDOMINAL PAIN

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Introduction: Abdominal pain is the most common symptom among children¹⁻³. The prevalence rates of abdominal pain in the USA and Europe generally range from 0.3% to 19.0%⁴. Persistent abdominal pain in children can limit children's daily activities and is associated with absence from school, lower quality of life, poor family functioning, and parental stress⁵⁻⁷. A better understanding of the pathophysiology and clinical characteristics of children's abdominal pain is significant for the appropriate management of the patients. To date, it has been reported that gastrointestinal symptoms are passed from one generation to another^{8,9}. However, studies that investigated the association between parents' morbidities and children's abdominal pain with big datasets are rare.

Aims & Methods: **Aims:** This study aimed to compare the frequencies of parents' morbidities between children with and without abdominal pain and to elucidate the effect of parents' morbidities on children's abdominal pain using the big dataset.

Methods: The Born in Bradford (BiB) cohort is a birth cohort study established in 2007 to understand and improve the health and wellbeing of children in Bradford. Between 2007 and 2011, 12,453 pregnant women (recruited at 26 - 28 weeks) with 13, 776 pregnancies, and 3,448 of their partners were recruited¹⁰⁻¹².

From the BiB cohort, we extracted patients and performed case-control studies with the adjustment of children's backgrounds (age, gender, ethnicity, and morbidities) by propensity score matching (case: children with abdominal pain vs control: children without abdominal pain, the average age of children was 5.3 ± 3.2 years old). Patients' morbidities were investigated using the disease codes assigned by their general practitioners. The frequencies of mothers' and fathers' comorbidities were compared between the 2 groups.

Results: Case-control study 1: frequency of mothers' morbidities

Children with abdominal pain (n=1,271) vs Children without abdominal pain (n=1,271)

The frequencies of mothers' abdominal pain (49.8% vs 35.2%, $p < 0.01$), gastro-oesophageal reflux disease (13.5% vs 9.7%, $p < 0.01$), depressive disorder (21.7% vs 17.0%, $p < 0.01$), arthritis (8.4% vs 5.2%, $p < 0.01$), and migraine (22.4% vs 16.3%, $p < 0.01$) were significantly higher in the case group compared with control group.

Case-control study 2: frequency of fathers' morbidities

Children with abdominal pain (n=272) vs Children without abdominal pain (n=272)

The frequency of migraine (11.4% vs 5.5%, $p = 0.02$) was significantly higher in the case vs control group. The frequencies of other morbidities were not significantly different between the 2 groups.

Conclusion: Mothers' GI morbidities, depressive disorder, and somatic pain and fathers' migraine were more frequently seen in children with abdominal pain. Parents' pain and psychiatric condition might affect the development of abdominal pain in children. Compared to fathers, the association between mothers' morbidities and their children's abdominal pain was more evident. Clinical assessment of children with abdominal pain should include an assessment of comorbidities in mothers as well in future studies.

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P0765

FACTORS ASSOCIATED WITH SELF-REPORTED CONSTIPATION SEVERITY IN NON-DIARRHEIC PATIENTS

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Introduction: Constipation is a common complaint of patients with functional bowel disorders (FBD). The present study aimed to evaluate the relationship between the self-reported constipation severity with demographics, clinical, physiological, and psychological parameters in non-diarrheic FBD patients.

Aims & Methods: 577 non-diarrheic FBD patients were included and had clinical, physiological, and psychological evaluation. The self-reported severity of constipation was analyzed using stepwise linear regression in the total population and within each clinical group.

Results: The patients were mainly of female gender (78 %) and were 48.3 ± 16.8 years old. They complained of IBS (55%), and 62% had defecation disorders. Depression scale was abnormal in 257 patients (45%). The relationships of the constipation severity varied according to the Rome IV phenotype. It was positively associated with oro-anal transit time in the phenotypes IBS-Constipation and defecation disorders, and negatively with Bristol stool form in IBS-Constipation, IBS-Mixed, Functional constipation, and defecation disorders. Additional associations with the severity of bloating, abdominal pain, age, or depression were also found for some phenotypes.

Conclusion: Our data support the hypothesis that constipation severity is associated with psychological, clinical, and physiological factors but the relationships with these factors vary according to clinical phenotypes.

Disclosure: Nothing to disclose

P0766

HIGH RESOLUTION ANORECTAL MANOMETRY IN PAEDIATRICS: VALUES FOR NORMALITY

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Introduction: Constipation (O) and fecal incontinence (IF) are frequent conditions worldwide, impacting both children as their families and health systems.

Since 2016, a consensus produced by ANMS-NASPGHAN has standardized practice in manometry anorectal (MAR), despite this there are still no guidelines on how to perform the exam. This year BSPGHAN — Motility Working Group (MWG) developed its guideline for the use of MAR in children with O and / or IF, recommending normal values according to the study by Banasiuk et al 2016.

One of the great challenges in this technique continues to be the lack of normal values for children, there are only 3 applicable studies.

Aims & Methods: To characterize the manometric findings according to the 3 studies available.

Retrospective study of MAR exams performed on children from 2017 to 2019, the exam was performed by the same operator with high resolution perfusion MAR catheter (MMS catheter G-88485). The results were analyzed according to the parameters mentioned by Athanasakos et al 2020 and the values of normality according to Banasiuk et al 2016 (3D solid state probe) - group 1; Carrington et al 2014 (probe solid state) and Kumar et al 2009 (perfusion catheter) - group 2.

Results: 12 patients, 58% male (n = 7), median age 9 years, underwent the examination in 67%

of the cases by O (n = 8), 25% by IF (n = 3) and 8% by anal pain (n = 1).

According to the parameters of group 1, almost all patients (92%, n = 11) presented resting hypotonia and in 50% had hypotonia in voluntary contraction (n = 6). According to parameters of group 2, only 50% (n = 6) had changes in resting pressure, with 33% hypotonia (n = 4) and 17% for hypertonia (n = 2), and only 1 presented hypotonia in voluntary contraction. All patients had an inhibitory anorectal reflex in the presence of these different thresholds and the cough reflex. The vast majority (81%, n = 9/11) presented some type of dyskinesia: Type 3 in 54% (n = 6/11) and the rest (type 1,2,4: n = 1/1/1) in 9% of cases.

Evaluating the rectal sensitivity, patients with O (88%, n = 7/8) were the most affected, mainly due to hyposensitivity.

Conclusion: The high discrepancy between the groups regarding the values of pressure at rest and voluntary contraction, it is probably because they are different probes, and in our group the variation of normality meets the parameters foreseen in group 2.

Management in the presence of these different thresholds becomes challenging for the institution of therapeutic plan, namely in patients with hypotonia for sessions of biofeedback or as in patients with hypertonia for therapy with botulinum toxin, which can be not feasible if there is an incorrect classification of the anal tonus.

This highlights the need for alert when applying these new recommendations, baseline studies and their respective protocols must be taken into account.

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Disclosure: Nothing to disclose

P0767

BLUNTED COLONIC FED RESPONSE IN SLOW TRANSIT CONSTIPATION COMPARED TO NORMAL TRANSIT PATIENTS MEASURED BY AMBULATORY WIRELESS MOTILITY CAPSULE

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Introduction: The colonic fed response is an increased contractile activity after the ingestion of a meal, also known as the gastrocolic reflex. Standard pan colonic manometry demonstrates impaired colonic response in patients with slow transit constipation (Rao et al. AJG 2004). Wireless Motility Capsule (WMC) detects a small bowel fed response to a standardized nutrient meal in healthy volunteers and constipated subjects, and shows the response is blunted in subjects with gastroparesis suggesting the ability of WMC to supplant cumbersome traditional manometry (Surjanhata et al. NGM 2017). But A gastro-colic reflex has not yet been reported with WMC.

Aims & Methods: This study evaluates the gastro-colic reflex detected with WMC in patients with UGI symptoms and who have normal or slow transit constipation. Subjects grouped by colonic transit (CTT) time, slow transit constipation (WMC colonic transit time (CTT) > 59 hrs) and normal colonic transit (CTT < 59 hrs) ingested 250 cc Ensure® meal (Abbott Laboratories, Illinois, USA) (250 ml, 250 kcal, protein 9 g, carbohydrates 40 g, fat 6 gram, fiber 0 g) after an 8 hour fast following WMC ingestion. Contraction frequency (Ct), pressure contraction area under the curve (AUC) and motility index (MI) were compared for 20 minutes pre-prandial baseline versus three consecutive 20-minute postprandial windows with paired T test. Significance was determined with p < 0.05.

Results: Fourteen subjects (9 normal colonic transit and 5 slow transit constipation) were analyzed. (Table 1) WMC detected increased contractile activity (Ct and MI) postprandially 0-40 min after meal ingestion compared to a pre-prandial baseline in the overall group and in the subgroup with normal colonic transit. Subjects with slow transit constipation patients failed to increase their motility activity significantly in all parameters after the meal.

Conclusion: Ambulatory WMC is able to detect a gastro-colic reflex to a standardized meal in subjects with normal colonic transit. This response is impaired in those with slow transit constipation, suggesting a neuro-pathic mechanism in the colon that can be detected in a non-invasive and ambulatory manner. Knowledge of a patient's colonic fed response could be useful information in understanding dysmotility beyond assessment of transit time alone.

Disclosure: Jack Semler - consultant for Medtronic Braden Kuo - clinical trial for Medtronic

	Preprandial	Postprandial		
	(-30 to -10 min)	(0 to +20 min)	(+20 to +40 min)	(+40 to +60 min)
	Overall			
Mean Ct (p-value)	25	68 (0.01)	59 (0.01)	42 (0.08)
Mean AUC (p-value)	1114	2572 (0.04)	2048 (0.09)	1806 (0.16)
Mean MI (p-value)	8.48	10.88 (0.02)	10.67 (0.02)	10.17 (0.08)
	Normal Colonic Transit			
Mean Ct (p-value)	29	82 (0.02)	69 (0.01)	43 (0.17)
Mean AUC (p-value)	1361	3221 (0.04)	2330 (0.16)	2108 (0.30)
Mean MI (p-value)	9.45	11.43 (0.01)	11.26 (<0.01)	10.46 (0.14)
	Slow Colonic Transit			
Mean Ct (p-value)	18	36 (0.41)	31 (0.57)	41 (0.28)
Mean AUC (p-value)	682	1059 (0.60)	1295 (0.50)	1429 (0.22)
Mean MI (p-value)	6.77	9.62 (0.27)	9.09 (0.36)	9.80 (0.17)

[Table 1]

P0768

EFFICACY OF AMITRIPTYLINE IN PEDIATRIC FUNCTIONAL ABDOMINAL PAIN DISORDERS: PLACEBO-CONTROLLED, RANDOMIZED, OPEN-LABELLED TRIAL

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Introduction: Anti-depressants, especially amitriptyline have a proven role in improving symptoms of functional abdominal pain disorders (FAPD) in adults. However, the pediatric studies showed variable results

Aims & Methods: The aim of this study was to evaluate the efficacy of amitriptyline in FAPD in children. In this placebo-controlled, open-labelled randomised trial, children (6 to 18 years of age) diagnosed as FAPD [functional dyspepsia (FD) (n=23), irritable bowel syndrome (IBS) (n=39), functional abdominal pain not otherwise specified (FAP-NOS) (n=127) and abdominal migraine (AM) (n=0), more than 1 diagnosis (n=5)] based on ROME IV criteria were randomised to either amitriptyline group (10 mg for < 35 kg and 25 mg for > 35 kg for 12 weeks) or placebo group. Post-treatment (12 weeks) improvement of pain scores (intensity, duration and frequency) and quality of life (QOL) from the baseline (4 weeks) were compared between two groups

Results: A total 194 children enrolled in the study [105 boys, mean age 11.25 (± 3.51) years] of which 149 completed the study and analysed (amitriptyline 75, placebo 74). There was significant difference in pain improvement in terms of percentage reduction of intensity (64% vs. 11%), frequency (61.4% vs. 5.3%), duration (64.3% vs. 7.7%) and percentage improvement in quality of life (78.1% vs. 28.4%) between amitriptyline and placebo group (p < 0.001 in all). On categorizing the percentage reduction in pain scores (sum of intensity, duration and frequency scores) good improvement (>50% reduction) was seen in 57/75 (76%) in amitriptyline

group compared to 9/74 (12.1%) in placebo ($p < 0.001$). Though improvement in pain scores were seen in children with IBS ($p = 0.01$) and FAP-NOS ($p < 0.001$), it was not significant in FD ($p = 0.086$). Adverse events (none were serious) noted in 19 (24%) children in amitriptyline group versus 10 (13.5%) in placebo group ($p = 0.07$)

Mean percentage ($\pm$ SD) changes in parameters from baseline	Amitriptyline (n=75)	Placebo (n=74)	P value
Pain Intensity	64.02 $\pm$ 46.8	11.0 $\pm$ 49.6	<0.001
Pain frequency	61.46 $\pm$ 40.64	5.31 $\pm$ 63.03	<0.001
Pain duration	64.33 $\pm$ 38.23	7.68 $\pm$ 68.70	<0.001
Quality of Life	79.11 $\pm$ 38.88	28.41 $\pm$ 63.06	<0.001
Total Pain scores (Intensity + duration + frequency)	64.31 $\pm$ 36.94	13.97 $\pm$ 46.93	<0.001
Occasions requiring analgesics	33.06 $\pm$ 26.31	22.61 $\pm$ 26.13	0.017

[Comparisons of change in pain, quality of life and analgesic requirement from baseline to 12 weeks post-treatment between amitriptyline and placebo]

Conclusion: A three-month trial of amitriptyline is significantly more effective in reducing the pain and improving quality of life in children with functional abdominal pain disorders. The safety profile of the drug and its efficacy necessitate for more frequent use in clinical setting.

Disclosure: Nothing to disclose

P0769

BEYOND ROME IV; CAN NALDEMEDINE CHANGE EXPECTATIONS OF TREATMENT RESPONSE IN OPIOID INDUCED CONSTIPATION?

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Introduction: Opioid-induced constipation (OIC) affects the majority of patients receiving opioids for either cancer pain or chronic non-cancer pain, reducing productivity, quality of life (QoL), and increasing health-care utilisation. Mainstay laxative treatments have questionable efficacy and cause side-effects in most patients, driving dissatisfaction and poor opioid adherence in many. Under-recognition and suboptimal treatment of OIC led the Rome process to systematise its definition. The emphasis of the Rome IV criteria on spontaneous bowel movements (SBMs) frequency of < 3 per week shapes regulatory guidelines for efficacy definition in clinical trials for OIC. Recent health technology appraisals note heterogeneity in responder populations of pivotal trials, suggesting the current response definition is insensitive to capturing the full benefits of effective treatments. Even among 'non-OIC' patients, more than two-thirds regard having one additional weekly BM as either very or extremely important. In this study we evaluated responder heterogeneity in *post hoc* analysis of data from the COMPOSE trials which evaluated the efficacy and safety of naldemedine (NLD) versus placebo (PLB) in different scenarios, to understand whether the definition of response captures all the clinical benefits of OIC treatment

Aims & Methods: We analysed the pooled intention-to-treat populations of the 12-week COMPOSE-1 & -2 (C1&2) randomised controlled trials (RCTs), as well as that of the 52-week COMPOSE-3 RCT (C3), published previously. For the C1&2 analysis we evaluated treatment response at Weeks 4, 8, and 12 using logistic regression to identify predictors of response, and

the Student's t-test to compare change from baseline (CFB) in SBMs, PAC-SYM, PAC-QOL, and derived EQ-5D health-related utility between responders to either NLD or PLB. Durability of treatment response was also determined. For the C3 analysis we evaluated treatment response at quarterly intervals from Week 12 through Week 52

Results: In C1&2 (n=1,088), 51% of treated patients responded at Week 4, while in C3 (n=1,240), 59% of treated patients did so. There were no meaningful differences in age at enrolment, gender balance, or baseline SBM frequency between responders and non-responders in either study population. After adjusting for age, gender, baseline SBMs, and opioid dose, the odds of treatment response by Week 4 in C1&2 was 2.2-fold greater for NLD patients (95% CI 1.82-2.76; $p < 0.001$), with $> 90\%$ durability at Weeks 8 and 12. In C3 the odds of response for NLD at Week 12 were 1.43 times greater (1.18-1.74) than PLB. In C1&2, by Week 12, NLD responders reported a CFB of +5.1 SBMs (SD 3.2) compared to PLB responders (+4.2 [2.5]; $p < 0.001$), a treatment effect of +0.91 SBMs. C3 PAC-QOL-Overall score CFB for Week 12 NLD responders showed greater improvement than PLB (-1.29 vs. -0.95; $p < 0.001$), a difference maintained in the stable laxative subgroup. Utility values showed consistent treatment benefit for NLD responders over PLB responders. In C1&2, this was 0.038 units at Week 4 and 0.033 at Week 12, while in C3 the difference was 0.041, 0.038, 0.058, and 0.040 at Weeks 12, 24, 36 and 52 respectively ($p < 0.01$ at all time points).

Conclusion: In RCTs, NLD elicited not only a higher likelihood of durable treatment response than PLB in OIC but it also conferred a higher quality of response measured either by stool frequency, symptom control, or health related QoL up to 52 weeks' treatment. The established definition of efficacy in OIC may not fully capture the benefit of effective treatments.

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P0770

ASSESSING THE PREVALENCE OF POSITIVE HYDROGEN BREATH TESTS IN PATIENTS REFERRED TO A TERTIARY UNIT, WITH SPECIAL ATTENTION TO HYPERMOBILE EHLERS-DANLOS SYNDROME

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Introduction: Hydrogen breath testing (HBT) is often used to diagnose small intestinal bacterial overgrowth (SIBO), however their specificity and sensitivity is poor and their role in the clinical management of patients with functional and motility disorders affecting the gut is controversial.¹ It is known that patients with certain conditions are at higher risk of developing SIBO; however there is little evidence of its prevalence in congenital connective tissue disorders, particularly hypermobility Ehlers-Danlos (hEDS).

Aims & Methods: We aimed to assess retrospectively the prevalence of SIBO in patients referred to a tertiary motility laboratory and compare results between different underlying condition subtype.

Consecutive patients referred to UCLH GI Physiology Unit for a HBT from January 2017 to January 2020 were included in the study. Patients typically presented with chronic (> 3 months) lower GI symptoms. Glucose HBT was conducted as per published standard recommendations (Rezaie et al. 2017). Patients were classified in the following groups according to the most relevant diagnosis for referral: functional colorectal disorders; GI mucosal injury (i.e Crohn's disease or Celiac disease), Systemic & Neurological Disorders (i.e diabetes mellitus, radiation enteritis) and hEDS. We also aimed to evaluate the role of PPIs on influencing a positive HBT di-

agnosis. Descriptive statistics and median with interquartile ranges were used to describe the patient groups. Chi-Squared test was used to identify significance of long-term PPI use on obtaining a positive HBT.

Results: Over the 3-year period, a total of 1,064 HBT were performed. Seventy percent were female, with median age of patients being 47 (35- 60) years. Only, 7.1% (76/1064) patients were diagnosed as having a positive HBT. Prevalence of positive HBT was highest in patients with Systemic & Neurological disorders (15.6%), followed by GI mucosal injury (13.1%) and functional symptoms (3.3%). None of the hEDS patients tested positive for HBT (Table 1). A total of 454 patients had PPI usage recorded, with 167 of these patients (21.1%) fulfilling the criteria for long-term PPI use. Patients on PPIs were more likely to have a positive HBT than patients off PPI (12.5% vs 5.3%; $p < 0.0001$)

Conclusion: Patients with functional GI colorectal disorders and, in particular patients with hEDS, have a low prevalence of SIBO. Patients on PPIs are more likely to have a positive glucose HBT compared to those that are not. Despite their symptom burden, diagnostic yield of HBT needs to be taken into consideration in patients with functional colorectal disorders and hEDS.

Patient Group	Functional	N (Valid)	Gender [female (n, %)]	Age (years) [Median (IQR 25- 75 percentiles)]	Negative Test (n)	Positive Test (n)	Percentage Positive/ N*100
		641	470 (73.3%)	43 (34.0-57.0)	620	21	3.28%
	GI Disease/ Gut Injury	258	169 (65.5%)	52.0 (36.0-65.0)	224	34	13.12%
	Systemic & Neurological Disorders	135	79 (58.5%)	54.0 (39.0- 64.0)	114	21	15.56%
	hEDS/JHS	30	27 (90%)	40.5 (27.75- 47.25)	30	0	0%
Total		1064	745 (70.0%)	47.0 (35.0-60.0)	987	76	7.14%

[Demographics of each patient group]

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Disclosure: Nothing to disclose

P0771

NOVEL ANALYSIS OF HIGH-RESOLUTION ANORECTAL MANOMETRY STUDIES REVEALS COUGH-ANORECTAL PRESSURE RESPONSES DIFFER BETWEEN HEALTHY NULLIPAROUS AND PAROUS INDIVIDUALS AND FAECAL INCONTINENCE

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Introduction: Anal resting pressure (RP) and squeeze pressure (SP) are the most frequently reported manometric measures of sphincter dysfunction¹. Though these 'traditional' measures are generally reduced in faecal incontinence (FI), only a proportion of patients fall outside the normal range. The cough-anorectal pressure response is frequently assessed as part of a routine manometric investigation but has not been the subject of detailed analysis in recent literature and the impact of parity is unknown.

Aims & Methods: The aim of this study was to evaluate anorectal pressure responses to coughing in healthy volunteers and to evaluate the impact of parity and FI on measurements. High-resolution anorectal manometry (HR-ARM) traces of 25 nulliparous (NP) and 25 parous (P) healthy volunteers, and 57 patients with FI were reviewed. Cough-anorectal pressure responses were analysed using novel qualitative and quantitative approaches and the results compared between groups. In FI, comparison against the 5th percentile in health was performed for relevant variables.

Results: Traditional measures were similar between NP and P women and lowest in FI (Table 1). Nulliparous HV (mean 36 years, 95% CI: 31-41) were significantly younger than parous HV (46, 95% CI: 42-50, $p < 0.05$) and FI patients (47, 95% CI: 43-50, $p < 0.001$). Maximum anal pressure and duration of the pressure response were greater in the anal canal than in the rectum in 98% of healthy volunteers, but only 79% of patients ($p = 0.0025$). The maximum anal increment during cough exceeded the rectal increment in 58% of healthy individuals and 44% of FI. The incremental anal-rectal pressure difference during cough was greater in NP women (42 mmHg, 95% CI: 21-64) compared to P women (6 mmHg (-14-25), $p < 0.036$) and FI (-2 mmHg (-15 -12), $p < 0.001$), but similar between P volunteers and FI. Qualitatively, six 'prototype' morphologies of the cough-anorectal response were conceived; pressurisation resembling a 'spear' limited to the upper anal canal was observed uniquely in FI. Considering all types of measures, of the 25 patients with normal RP and SP, cough parameters were abnormal in 13 (52%).

	Nulliparous	Parous	FI
Resting pressure (mmHg)	67 (59-76)	69 (62-77)	58 (52-65)
Squeeze increment (mmHg)	202 (170-234)	164 (132-197)	78 (61-95) †§
Maximum rectal increment during cough	85 (73-97)	94 (78-110)	70 (61-79) ¶
Maximum anal increment during cough	127 (104-150)	100 (76-124)	68 (56-81) † ¶
Incremental anal-rectal pressure difference	42 (21-64) *	6 (-14-25)	-2 (-15-12) †
Rectal pressure duration (sec)	1.0 (0.9-1.1)	1.0 (0.9-1.2)	0.9 (0.8-1.1)
Anal pressure duration (sec)	2.3 (1.8-2.7)	2.3 (1.8-2.7)	1.5 (1.3-1.8) ‡
Anal-rectal duration difference (sec)	1.2 (0.8-1.7)	1.0 (0.7-1.2)	0.6 (0.4-0.8) ‡

*Nulliparous vs Parous $p < 0.05$, †FI vs Nulliparous $p \leq 0.001$, ‡FI vs Nulliparous $p \leq 0.01$, §FI vs Parous $p \leq 0.001$, ¶FI vs Parous $p < 0.05$

[Cough parameters (mean and 95% CI) in nulliparous and parous HV and FI patients]

Conclusion: From HR-ARM recordings, novel cough measures showed differences in anal function between NP and P women and patients with FI. Additionally, a proportion of patients were found to have an 'isolated' cough abnormality that was not revealed by use of 'traditional' measures (rest and squeeze) alone. An abnormal cough may be considered one with one or more of the following features: a 'spear' (upper anal canal) morphology, greater maximum rectal than anal pressure, or below the 5th percentile (derived from health) for anal duration, anal-rectal duration difference, maximum anal increment, or maximum anal-rectal incremental pressure difference. Cough metrics are shown to increase manometric yield, though clinical utility will require assessment by longitudinal studies.

References: 1. Carrington EV et al. Methods of anorectal manometry vary widely in clinical practice: Results from an international survey. Neurogastroenterol Motil. 2017;29(8):e13016.

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P0772 WITHDRAWN

P0773

PREVALENCE OF IRRITABLE BOWEL SYNDROME IN BULGARIA: A POPULATION-BASED STUDY

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Introduction: The prevalence of irritable bowel syndrome (IBS), according to geographic location, has been recently well-reported. However, more population-based studies are needed, especially in geographical regions lacking epidemiological data on the prevalence of IBS, such as Eastern Europe, particularly Bulgaria.

Aims & Methods: We aimed to evaluate the prevalence of IBS in the Bulgarian population and to assess the risk factors associated with this disorder. We sent an internet-based cross-sectional health survey to Bulgarian adults, 18 to 65 years old. Individuals were invited to complete an online questionnaire on general health without mention that the purpose of this survey was to examine gastrointestinal symptoms. The survey collected data on socio-demographic, behavioral and lifestyle characteristics, and diagnostic questions following Rome IV criteria to assess IBS occurrence. The difference in IBS prevalence by drinking and smoking habits, occupation, education level, urinary problems, sexual problems, milk intolerance, and overlap with functional dyspepsia (FD) was assessed.

Results: Data was collected from 1896 individuals (mean age = 35.5 years, SD = 11.7), 73.1% females. The prevalence of IBS in the study population according to Rome IV criteria was 20% (2.8% were with predominant constipation - IBS-C, 6.4% with predominant diarrhea - IBS-D, 10.4 % had IBS with mixed bowel habits - IBS-M, and 0.4% unclassified IBS - U). Sex ($p=0.005$), age ($p<0.001$), marital status ($p=0.009$), occupation ($p=0.001$), alcohol consumption ($p=0.013$), sexual problems ($p<0.001$), overlap with FD ($p<0.001$), and milk intolerance ($p<0.001$) were significantly associated with IBS prevalence. Females ($p=0.032$; OR 1.50), patients with FD ($p<0.001$; OR 104.98), sexual problems ($p=0.001$; OR 1.55), and milk intolerance ($p<0.001$; OR 2.22) are at a higher risk of having IBS.

Conclusion: The first data on IBS prevalence in the adult population in Bulgaria has been reported. IBS prevalence shows differing associations, suggesting differences in pathophysiological processes or influences.

Disclosure: Nothing to disclose

P0774 WITHDRAWN

P0775

PREVALENCE OF ROME IV CRITERIA FOR IRRITABLE BOWEL SYNDROME AND RED FLAG SYMPTOMS IN VISITORS OF A PATIENT CENTERED INFORMATIVE WEBSITE

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Introduction: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain and changes in stool pattern. Based on dominant stool pattern we can subtype into IBS-D (diarrhea), IBS-C (constipation), IBS-M (mixed) or IBS-U (unspecified). Many undiagnosed patients experiencing chronic abdominal complaints do not immediately visit a health care professional but turn to the internet for advice. Therefore, we probably underestimate the prevalence of disorders like IBS. Furthermore, when these patients do not visit a doctor, red flag symptoms are not noticed, and more serious diseases could be missed.

Aims & Methods: The aim of this study was to assess the prevalence of Rome IV criteria for IBS and red flag symptoms in a population visiting an IBS patient centered informative website. Visitors of the website had the opportunity to participate in a questionnaire combining the Rome IV criteria and red flags (blood in stool, weight loss, start symptoms after 50 years of age, family history of colon cancer, unexplained fever). Afterwards, they received the results of the Rome IV criteria and the presence of red flag symptoms via mail. After informed consent the data was extracted, and the prevalence of positive Rome IV criteria and red flag symptoms was calculated.

Results: 62 visitors completed the questionnaire and 56 visitors (90.3%) gave permission to use the data for research purposes. Of these 56 visitors, 35 fulfilled the Rome IV criteria (62.5%). Based on stool pattern 11 were IBS-D (31.4%), 7 IBS-C (20.0%), 15 IBS-M (42.9%) and 2 IBS-U (5.7%). Of the visitors not fulfilling the Rome IV criteria this was due to (multiple reasons possible): insufficient abdominal pain (40.9%), insufficient changes in stool pattern (40.9%) or symptoms shorter than 6 months (40.9%). 20 visitors had red flags (35.7%): 8.9% had bloody stools, 16.1% unexplained weight loss, 3.6% unexplained fever, 12.5% a positive family history for colon cancer and 5.4% were older than 50 years when symptoms started. Patients fulfilling the Rome IV criteria had a higher percentage of red flags compared to Rome IV negative patients (42.9% versus 23.8%).

Conclusion: Since the COVID-19 pandemic there has been an increasing interest in telemedicine. Based on our research results, we believe digital questionnaires could aid in the screening of patients presenting with abdominal symptoms. Since more than a third of our population has at least one red flag symptom we think patient centered website could also help raise awareness and direct patients at risk towards consulting a health care professional. Furthermore, by quickly identifying the presence of red flag symptoms we can pinpoint the patients needing more extensive examinations, like an endoscopy, faster.

Disclosure: Nothing to disclose

P0776

ECONOMIC BURDEN IN PRIMARY CARE IRRITABLE BOWEL SYNDROME PATIENTS FULFILLING ROME IV CRITERIA

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Introduction: Irritable bowel syndrome (IBS) is one of the most common conditions encountered in clinical practice, not only by gastroenterologists but also in primary care. IBS patients fulfilling the Rome IV criteria (Rome+) are characterized by a higher symptom severity compared to IBS patients not fulfilling Rome IV (Rome-), but data on their economic impact at primary care level is still lacking.

Aims & Methods: Our aim was to evaluate the economic impact in primary care Rome+ and compare to Rome- IBS patients.

Newly diagnosed IBS patients were recruited by 67 primary care physicians. Patients completed the Rome IV questionnaire and questions regarding their demographic characteristics and stool types. In addition, the economic impact was collected using a Health Resource Utilisation (HRU) and Work Productivity and Activity Impairment (WPAI) questionnaire, assessing self-cost, healthcare utilization and absence at work related to IBS. The impact of IBS symptoms on the productivity and on daily activities was evaluated based on a scale from 0 (no effect) to 10 (IBS symptoms completely prevented me). Data were compared in Rome+ and Rome- patients using non-parametric statistical tests, Mann-Whitney test, and Chi square test.

Results: In 426 primary care IBS patients (41.0±1 years, 75% females), the stool subtype distribution was: 21% constipation, 28% diarrhea, 39% mixed, and 12% unclassified. Seventy percent of the patients fulfilled the Rome IV criteria (Rome+). In the previous 3 months, 31% of Rome+ patients used over-the-counter medication, compared to 20% Rome- patients (p=0.03). A significant difference was found for intake of fiber supplements and bulk laxatives in Rome+ compared to Rome- (both p=0.04). Of the IBS patients who are currently employed (65% Rome- and 72% Rome+), respectively, 7% and 19% were absent from work in the previous 6 months because of IBS (p=0.01). Respectively, 33% and 51% of the Rome- and Rome+ patients experienced impaired working capacity because of their IBS symptoms (p=0.005). The productivity (p=0.0001) and ability to do regular daily activities (p< 0.0001) were significantly more affected in the Rome+ (3.2±0.2 and 3.6±0.1) group compared to Rome- (1.9±0.3 and 2.5±0.2).

Conclusion: In a large primary care IBS cohort, a high percentage fulfil Rome IV criteria, and these are characterized by a higher economic burden due to a higher self-medication use and more absence from work compared to patients not fulfilling Rome IV. In addition, their productivity at work and daily activities are more affected by their IBS symptoms.

Disclosure: Nothing to disclose

P0777

DAILY SYMPTOMS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME: A 2-WEEK PROSPECTIVE HOURLY EVALUATION

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Introduction: Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders, characterized by a combination of abdominal pain and abnormal bowel habits. In the recent Rome IV criteria, the defining criteria for IBS changed from 'abdominal pain that improves with defecation' to 'abdominal pain that is related to defecation'. Moreover, meal intake is also a potential trigger for IBS symptoms. However, few studies have prospectively addressed the association between abdominal pain, meal intake and other key symptoms in IBS.

Aims & Methods: For a period of two weeks, patients with IBS of all subtypes prospectively registered their patterns of meal intake, bowel habits (defecation frequency and Bristol Stool Form (BSF) scale), abdominal pain, nausea and bloating on an hourly basis by use of a validated diary¹. We aimed to identify the effect of defecation and meal intake on the occurrence or relief of registered symptoms. Hence, temporal associations between these (binary) variables were computed and expressed as standardised β s, which allowed us to compare relative effects. The standardized β s coefficient expresses the effect of a single standardized deviation change. Statistical significance was assessed with adjustment for reverse causation and confounding by time of the day. Briefly, the principle of the method is that it uses the actual data to simulate the null-distribution, instead of modelling it using common statistical parameters. This approach allows customized adjustments for confounders and is free from assumptions.

Results: Three hundred IBS patients [198 female, aged 38 (range 19-72) years] completed the 2-week daily diary symptom registration.

Meal intake was significantly associated with the occurrence of abdominal pain (β 0.28; p< 0.001), bloating (β 0.48; p< 0.001), nausea (β 0.16; p< 0.01), and defecation (β 0.58; p< 0.001) in the 2 hours following food intake. Except for a stronger association between meal intake and the occurrence of defecation in patients having IBS with diarrhoea (β 0.8; p(interaction)=0.03), no significant differences among IBS subtypes were found.

In general, defecation was associated with abdominal pain relief (β -0.17; p< 0.01) approximately twice as often as it was associated with the occurrence of abdominal pain, with no differences between IBS subtypes. Defecation with loose stool was associated with relief of abdominal pain (β -0.32; p< 0.01), unlike defecations with hard stool (β -0.02; p=0.85).

However, hard stools tended to relieve abdominal pain in IBS with constipation (β -0.4), and occurrence of pain in IBS with diarrhoea [β 0.4; p(interaction)=0.055]. Defecation following meal intake was more commonly associated with normal stool (BSF 3-5) than either loose (BSF 6-7) or hard (BSF 1-2) stool. Finally, defecation led to relief of bloating (β -0.29; p< 0.001), which was seen both for hard (β -0.21; p< 0.05) and loose stools (β -0.27; p< 0.05).

Conclusion: Meal intake and defecation are important physiological events modulating symptoms in IBS. Meal intake is a major trigger for the occurrence of abdominal pain, nausea, defecation and especially bloating. Defecation frequently leads to relief of bloating and is more likely to relieve rather than trigger pain, and this is especially true for defecation with loose stools.

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P0778

DAILY SYMPTOM PATTERNS IN IRRITABLE BOWEL SYNDROME (IBS): AN ALTERNATIVE WAY FOR CLASSIFICATION?

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Introduction: Traditionally, irritable bowel syndrome (IBS) has been subdivided into different subgroups based on the predominant stool pattern, i.e. IBS with predominant constipation (IBS-C) or diarrhoea (IBS-D), mixed bowel habits (IBS-M), or normal stool consistency (IBS-U). However, this categorisation gives limited attention to other key symptoms such as pain and bloating. Moreover, the current categorization may prove imperfect for identifying optimal treatment.

Aims & Methods: We aimed to identify different subgroups of IBS patients based on their daily symptom pattern of pain and bloating.

For two weeks, patients were asked to register meal intake, defecation, pain, nausea, bloating, and stool-associated symptoms on an hourly basis. Questionnaires to determine the severity of IBS symptoms (IBS-SSS), somatic symptoms (PHQ-15) and psychological distress (HAD) were used. Based on retrospective recall and a clinical history, patients were categorized according to Rome IV.

We performed a customised latent class analysis on the daily symptom patterns. Briefly, the analysis was designed diurnal patterns of when symptoms were present, rather than intensity of symptoms. We determined the number of classes (k) by simulation. We compared clinical outcomes across the latent classes using standard statistical methods.

Results: Three hundred IBS patients [198 female, aged 37 (range 19-72) years], finalized the two-week daily diary symptom registrations.

We identified subgroups based on pain and bloating patterns, respectively (both $p < 0.001$). The summary results for pain are presented in Table 1.

Pain subgroups	Continuous (n=94)	Evening (n=26)	Morning (n=35)	Incidental (n=145)	p<0.001
Age (years)	36	38	45	36	p=0.08
Gender (% female)	73	88	69	65	p=0.08
IBS-SSS (mean)	360	347	287	285	p<0.001
HAD - anxiety (mean)	8	7	7	7	p=0.53
HAD - depression (mean)	5	3	5	4	p=0.05
PHQ-15 (mean)	13.6	12.8	11.4	10.9	p<0.001
Stool freq/day	1.6	1.5	1.9	1.6	p=0.47
Bristol stool scale (mean)	4.1	3.6	4.0	3.9	p=0.37

[An alternative pain classification]

For the "continuous" subgroup, the event would have to be present for the majority of the day, whereas "evening" and "morning" subgroups only reported the symptoms during that time. The "incidental" subgroup, reported symptoms at different time points. For bloating, we found a comparable distribution with an additional mixed subgroup ($p < 0.001$).

All subgroups were overrepresented by females although significantly less in the morning predominant and incidental bloating subgroups ($p < 0.05$). Those with continuous pain and bloating showed overall more severe IBS (IBS-SSS) and somatic (PHQ-15) symptoms (both, $p < 0.001$). For pain, no differences among the traditional IBS subgroups were found, but for bloating, IBS-C and IBS-D differed in bloating patterns with a pattern of more continuous bloating in IBS-C and more incidental bloating in IBS-D ($p < 0.05$).

Conclusion: Different daily symptom patterns of pain and bloating can be identified in IBS. These subgroups show differences in symptom severity and could potentially provide an alternative for future classifications or patient treatment.

Disclosure: Nothing to disclose

P0779

THE GASTROINTESTINAL SYMPTOM PROFILE AMONG IRRITABLE BOWEL SYNDROME PATIENTS WITH VARYING DEGREES OF SOMATIC SYMPTOMS

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Introduction: Multiple somatic symptoms are common among patients with irritable bowel syndrome (IBS). Nevertheless, the association between the gastrointestinal symptom profile varying degrees of somatic symptoms in IBS patients is poorly understood.

Aims & Methods: We aimed to investigate the gastrointestinal symptom profiles among IBS patients with none/mild, moderate, and severe non-GI somatic symptoms. For two weeks, IBS patients prospectively registered their symptoms hourly in a diary. We performed a customised latent class analysis to detect diurnal patterns of when symptoms were present (rather than intensity of symptoms). The Patient Health Questionnaire (PHQ-15) was used to identify patients with no/mild, moderate, and severe somatic symptoms by using validated cut-off levels, and the GI symptom patterns from the latent class analysis were compared among these groups. Questionnaires were used to assess IBS symptom severity (IBS-SSS), and anxiety and depression (HADS-A and HADS-D). IBS subtypes were defined according to the Rome IV criteria.

Results: The study included 290 IBS patients; of these, 86 had no/mild, 125 patients moderate, and 79 severe somatic symptoms. With increasing severity of somatic symptoms there was a gradual increase in the proportion of females, IBS symptom severity, and anxiety/depression scores (Table 1).

When analysing diurnal symptom profiles, different profiles were identified among the somatic symptom severity groups, where IBS patients with moderate to severe somatic symptoms were more prone to continuous pain and bloating throughout the day (Table 1). Lastly, there was a gradual increase of patients reporting nausea with more somatic symptoms, 7/86 (8%) in the none/mild, 30/125 (25%) in the moderate and 31/78 (40%) in the severe somatic symptom group, $p < 0.001$.

Conclusion: IBS patients with severe somatic symptoms constitute a distinct group of patients with more females, more severe overall IBS symptoms, increased nausea, psychological distress, and a more continuous form of diurnal bloating and pain profile. This complex clinical picture needs to be taken into account to optimize clinical management of these patients.

Disclosure: Nothing to disclose

	None/Mild (N=86)	Moderate (N=125)	Severe (N=79)	p-value
Age	37.4 (27.6-51.9)	34.9 (28.3-46.0)	NS	
Females	45 (52%)	86 (69%)	72 (91%)	< 0.001
Subtype				
<i>IBS-C</i>	16 (21%)	30 (26%)	19 (25%)	NS
<i>IBS-D</i>	38 (49%)	40 (35%)	27 (35%)	NS
<i>IBS-M</i>	17 (22%)	38 (33%)	27 (35%)	0.095
<i>IBS-U</i>	7 (9%)	7 (6%)	4 (5%)	NS
IBS-SSS	285 (224-333)	316 (255-372)	362 (319-413)	< 0.001
HADS-A	5 (4-9)	7 (4-10)	10 (7-13)	< 0.001
HADS-D	3 (2-5)	5 (2-7)	7 (5-9)	< 0.001
Mean Bristol stool form	4.2 (3.4-4.8)	3.8 (3.0-4.8)	4.0 (3.0-5.1)	< 0.001
Diurnal symptom pattern - Pain				<0.001
<i>Continuous</i>	13 (15%)	43 (34%)	35 (45%)	
<i>Evening</i>	8 (9%)	7 (6%)	10 (13%)	
<i>Incidental</i>	54 (63%)	58 (46%)	27 (35%)	
<i>Morning</i>	11 (13%)	17 (14%)	6 (8%)	
Diurnal symptom pattern - Bloating				< 0.001
<i>Continuous</i>	14 (16%)	44 (35%)	36 (46%)	
<i>Evening</i>	7 (8%)	23 (18%)	11 (14%)	
<i>Incidental</i>	36 (42%)	24 (19%)	15 (19%)	
<i>Mixed</i>	17 (20%)	27 (22%)	11 (14%)	
<i>Morning</i>	12 (14%)	7 (6%)	5 (6%)	

[Table 1. Comparison of patients with none to severe somatic symptoms (PHQ-15). Results presented as median (interquartile range) or n (%).]

P0780

IBS SUBGROUPS: SIMILARITIES AND DIFFERENCES IN PROSPECTIVE DAILY SYMPTOM RECORDINGS DURING A TWO-WEEK PERIOD

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Introduction: Irritable bowel syndrome (IBS), a functional bowel disorder, characterized by abdominal pain and altered bowel habit, is one of the most common functional gastrointestinal disorders. In order to provide adequate treatment for these patients, patients are categorized based on their predominant stool pattern. However, differences and similarities in symptom patterns among these subgroups using prospective symptom assessments are missing.

Aims & Methods: For a period of two weeks, patients prospectively registered their meal intake, pain, nausea, bloating, defecations, and stool-associated symptoms on an hourly basis. We aimed to evaluate differences and similarities in the daily symptom pattern among IBS subgroups. Associations among these symptoms were determined. Based on retrospective recall and a clinical history, patients were categorized according to

Rome IV as IBS with predominant constipation (IBS-C) or diarrhoea (IBS-D), IBS with mixed bowel habits (IBS-M), or IBS unclassified (IBS-U). Questionnaires to determine the severity of IBS symptoms (IBS-SSS), somatic symptoms (PHQ-15) and psychological distress (HAD) were used. To evaluate these aims we used one-way ANOVA in R.

Results: Three hundred IBS patients [198 female, aged 37 (range 19-72)] (71 IBS-C, 105 IBS-D, 84 IBS-M, and 20 IBS-U), finalized the two-week daily diary symptom registrations and 171 underwent a one-week radiopaque marker study.

IBS-D was more prevalent in males, while IBS-C and IBS-M were more prevalent in females. Between these groups, no differences for age were found. These groups however differed in colonic transit time, defecation frequency, stool form (BSF), straining, and urgency, but not for overall symptom severity, somatic or psychological symptoms. No significant differences were found for pain, bloating or nausea associations with meal intake for either of the IBS subgroups. Likewise, IBS subgroups did not differ regarding the association between defecation, and pain or bloating. The summary results are presented in Table 1.

		IBS-C (n=71)	IBS-D (n=105)	IBS-M (n=84)	IBS-U (n=20)	P-value
	IBS-SSS (mean)	318	317	337	264	0.07
	HAD-anxiety (mean)	6	8	7	7	0.82
	HAD-depression (mean)	5	5	4	5.5	0.82
	PHQ15 (mean)	12.2	11.8	12.7	10.9	0.27
	Oroanal transit time (days)	2.2	1.0	1.4	1.6	<0.001
	BSF (mean)	3.2	4.7	3.6	3.7	<0.001
Meal association	Pain	0.28	0.40	0.18	0.19	0.29
	Bloating	0.51	0.61	0.37	0.35	0.22
	Nausea	0.11	0.15	0.26	-0.02	0.56
	Defecation freq	0.43	0.75	0.46	0.42	0.03
Stool association	Pain	-0.22	-0.19	-0.07	-0.21	0.82
	Bloating	-0.57	-0.17	-0.27	-0.24	0.16

[Irritable bowel syndrome subgroup differences]

Conclusion: IBS subgroups, as they are currently defined, differ predominantly in stool-associated symptoms, but not to any larger extent with other clinical features in IBS. Potentially, alternative ways to subgroup IBS patients may be more relevant to the overall IBS symptoms.

Disclosure: Nothing to disclose

P0781

THE ROLE OF BOWEL DIARIES IN THE GASTROENTEROLOGY EXTERNAL CONSULTATION

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Introduction: Gastrointestinal (GI) disorders, particularly functional GI disorders (FGIDs), are common diseases with predominantly clinical diagnostic criteria. The use of appropriate tools that objectify the patient's complaints may improve the care of these patients. Despite the potential

advantages of patients' self-recordings of bowel habits (BH), rare studies evaluate the relevance of clinical information obtained through bowel diaries in clinical practice.

Aims & Methods: The main objective of this study is to evaluate the role of the bowel diaries as a complement to the clinical interview for the diagnosis and management of FGIDs in a GI consultation. For a period of three months, patients were interviewed at the end of their GI consultation about their clinical history, BH and GI symptoms. The bowel diary was then filled by the patients at home for two weeks with record of BM, stool consistency, GI symptoms and relief medication. The data collected from the clinical interview and from the bowel diaries was compared.

Results: Fifty-three patients participated in the study. The frequency of bowel movements (BM) was significantly different ($p=0.007$) between the clinical interviews and bowel diaries of the patients, as the patients underestimated their number of BM in the interviews. There was only a minimal agreement between stool consistencies described in the interviews and recorded in the diaries ($\kappa = 0.281$). There was a significant difference ($p=0.012$) in straining between the interviews and diaries of the patients, as they overestimated their straining during evacuation in the interviews. Regarding the subgroups' analysis, patients with proctological disorders described less BM in their interviews ($p=0.033$). The description of straining during evacuation was overestimated in the interviews of patients without proctological disorders ($p=0.028$) and more educated patients ($p=0.028$).

Conclusion: Overall, there were discrepancies between the clinical interview and the bowel diary of the patients regarding the number of bowel movements, the stool consistency and straining. Thus, this simple and inexpensive tool has proved to be a potential added value in daily clinical practice, allowing to objectify complaints and consequently treat patients more adequately.

Disclosure: Nothing to disclose

P0782

GLUTEN-SENSITIVE IBS: A NEW ENTITY?

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Introduction: Irritable bowel syndrome (IBS) is one of the most common functional intestinal disorder. IBS-like symptoms are often part of the non-celiac gluten sensitive (NCGS) clinical picture. Recent studies support the hypothesis that gluten may trigger IBS-symptoms and evidences showed a significant overlap between these 2 entities.

Aims & Methods: Aim of the study was to assess the efficacy of a two months gluten-free diet in addition to rifaximin and FODMAP diet in improving IBS-like symptoms and quality of life.

The present study included 172 patients with IBS-predominant diarrhea (IBS-D) based on Rome IV criteria. Exclusion criteria: IgA deficiency, tTg-IgA positive. All patients received the same baseline treatment for two months: FODMAP diet and rifaximin 1200mg/day, 10 days/month. Patients were divided into two groups: control group (88 patients) which received only baseline treatment for two months and gluten-free diet group (84 patients) which had in addition to baseline treatment a gluten-free diet for two months.

Abdominal pain and bloating were assessed by visual analogue scale (VAS), stool consistency by Bristol Stool Form (BSF) and quality of life (QoL) by IBS-QoL (assessment was performed at baseline and after 2

months of treatment). Improvement in abdominal pain scores, bloating scores, stool consistency scores and quality of life scores at the end of the study was evaluated.

Results: Significantly more patients in the gluten-free diet group than in the control group had adequate improvement in abdominal pain scores (61.9% vs. 45.4%, $p<0.05$) and bloating scores (78.5% vs. 50%, $p<0.05$). Regarding stool consistency scores improvement, there was no statistical significant difference between the two groups (61.3% in the control group, respectively 59.5% in the gluten-free diet group, $p>0.05$). Patients in the gluten-free diet group compared to patients in the control group had a better quality of life after treatment (83.3% vs. 54.5%, $p<0.05$).

Conclusion: Gluten-free diet for two months in addition to rifaximin is effective in improving IBS-like symptoms and quality of life in patients with IBS-D and may also identify a part of patients which are misdiagnosed with IBS-D instead of NCGS or may emphasize the overlap between these two entities. The role of the dietary triggers in IBS is a topic of great interest and further studies are needed for a better understanding of the link or overlap between IBS and NCGS and for defining a new entity like gluten-sensitive IBS.

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P0783

FAECAL MICROBIOTA TRANSPLANTATION (FMT) RESTORES THE COLONIC ENTEROENDOCRINE CELLS DENSITY TO NORMAL LEVELS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: In a previous study from our group, FMT reduced symptoms and improved the quality of life in IBS patients (1). Patients with IBS have generally lower density of enteroendocrine cells (2). The enteroendocrine cells regulate gastrointestinal motility, visceral sensitivity and secretion (2). IBS patients exhibit gastrointestinal dysmotility, visceral hypersensitivity and abnormal intestinal secretion (2). It is believed, therefore, that the enteroendocrine cells play a certain role in the pathophysiology of IBS (2).

The present study was conducted to investigate whether the positive effects of FMT are associated with changes in the density of colonic enteroendocrine cells.

Aims & Methods: This study included 93 of the 164 IBS patients who participated in our previous study (1). They were belonging to three groups: placebo who received 30-g own faeces (24 patients), the group who received 30-g of super-donor faeces (47patients) and the group that received 60-g of super-donor faeces (22 patients). As a control group, 24 healthy subjects were included. The patients underwent sigmoidoscopy with biopsies and completed three questionnaires to assess their symptoms and quality of live at the baseline and at 1 month after FMT. The control group underwent sigmoidoscopy with biopsies. Abdominal symptoms, fatigue and quality of life were assessed by the IBS-SSS, fatigue Assessment Scale (FAS), IBS-Quality of Life questionnaires. The biopsy samples were immuno-stained for chromogranin A (a general marker for enteroendocrine cells), serotonin, polypeptide YY (PYY) and oxyntomodulin (enteroglucagon). The densities of these cells were quantified by computer image analysis.

Results: The densities of the enteroendocrine cells at the baseline and 1 month after FMT are presented in Table 1. The densities of chromogranin A, serotonin, PYY and enteroglucagon in the control group were 32±15 (mean±SD), 31±9, 12±6 and 15±10, respectively. The density of chromogranin A of IBS patients was significantly lower than that of controls. There was no difference between the density of chromogranin A between control group and 30-g group or 60-g group 1 month after FMT. The density of chromogranin A correlated inversely with the IBS-SSS and FAS scores ($r=-0.3$, $P<0.0001$ and $r=-0.2$, $P=0.02$, respectively). In non-responders, the cell density of Chromogranin A, serotonin, PYY and enteroglucagon at the baseline were 15±8, 7±3, 10±4 and 7±2, respectively. The corresponding figure 1 month after FMT were 23±11, 10±6, 12±7 and 19±10.

Conclusion: The present findings suggest that the effects of FMT on symptoms in IBS patients might be caused, at least partially, by its effect on enteroendocrine cells. In support of this assumption is the close correlation between the density of enteroendocrine cells and IBS symptoms.

Cell Type	Placebo		30-g group		60-g group		Responders	
	Base-line	1 month	Base-line	1 month	Base-line	1 month	Base-line	1 month
Chromogranin A	15±9	20±10	15±7	32±17****	15±5	30±11****	15±6	32±14****
Serotonin	6±3	7±5	7±4	11±7*	7±3	14±8*	7±3	11±7**
PYY	10±5	12±8	8±4	15±10****	7±3	18±8***	8±4	17±10****
Enteroglucagon	7±2	16±6	8±4	22±9****	7±3	23±10****	8±4	22±9****

[Table 1. The density of various colonic enteroendocrine cell types (mean±SD)]

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Disclosure: Nothing to disclose

P0784

SACCHAROMYCES CEREVISIAE CNCM I-3856 IN IBS WITH PREDOMINANT CONSTIPATION: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER CLINICAL TRIAL

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Introduction: Probiotics are a promising solution with potential for acting on the multifactorial causes and clinical symptoms of Irritable Bowel Syndrome (IBS).¹ Among them, *S.cerevisiae* CNCM I-3856 has already shown beneficial effects in IBS subjects, particularly in IBS with predominant constipation (IBS-C).^{2,3}

Aims & Methods: To evaluate the benefit of oral supplementation with *S.cerevisiae* CNCM I-3856 in 456 IBS subjects (64 male, 392 female) with predominant constipation matching Rome IV criteria⁴ and randomly assigned to the group receiving *S.cerevisiae* CNCM I-3856 (n=230, 8.10⁹ CFU/day) or the placebo (n=226). After a run-in period of 2 to 4 weeks, subjects joined the 8-week intervention and performed a daily evaluation of gastrointestinal symptoms. The primary objective was to evaluate the effect

of *S.cerevisiae* CNCM I-3856 on abdominal pain assessed through the area under the curve of abdominal pain score calculated using the mean daily score rated with a 7-point Likert scale over the last 4 weeks of the intervention period (AUC_{W5-W8}). Secondary objectives included the evaluation of the percentage of responders (defined as subjects experiencing a reduction of at least 30% of the baseline score of abdominal pain over the last 4 weeks of supplementation), quality of life (IBS-QoL questionnaire) administered at baseline and after 4 and 8 weeks of supplementation, bloating, flatulence/borborygmi, bowel movements frequency and stool consistency. Statistical analyses were performed on both ITT and PP populations.

Results: Abdominal pain evolution over the 8-week intervention period decreased similarly to previously reported results² with a more important but not significant difference of AUC_{W5-W8} in subjects receiving *S.cerevisiae* CNCM I-3856 vs placebo ($p=0.073$, [CI95%] = -0.59 [-1.23;0.05]). Secondary endpoints analyses demonstrated a statistically significant higher percentage of responders in the group supplemented with *S.cerevisiae* CNCM I-3856 (45.09% vs 33.94%, $p=0.017$). After 8 weeks of supplementation, overall IBS-QoL score was significantly higher in the active group in comparison with the placebo group ($p=0.047$, [CI95%] = 3.86 [0.52;7.20]), corresponding to a better body image score ($p=0.040$, [CI95%] = 3.96 [0.17;7.75]), a lower interference with activity ($p=0.044$, [CI95%] = 4.22 [0.62;7.83]) and a lower level of food avoidance ($p=0.030$, [CI95%] = 5.69 [1.10;10.28]). No statistically significant differences were reported on the evolution of bowel movements frequency and stool consistency between the groups. Similar data were obtained both in ITT and PP populations.

Conclusion: Daily administration of *S.cerevisiae* CNCM I-3856 reduces abdominal pain and improves the quality of life in IBS subjects with predominant constipation. With 3 clinical studies performed in over 1000 subjects with IBS, *S.cerevisiae* CNCM I-3856 appears as one of the most documented probiotic solution in this highly prevalent functional gastrointestinal disorder.⁵

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P0785 WITHDRAWN

P0786

PREDICTORS OF TREATMENT RESPONSE TO THE LOW FODMAP AND THE TRADITIONAL DIET IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: The NICE traditional diet for irritable bowel syndrome (IBS) patients and the low fermentable oligo-, di-, monosaccharides, and polyols (FODMAP) diet have shown efficacy in IBS. Predictors of dietary treatment response remain to be identified.

Aims & Methods: Therefore, we aimed to investigate psychological, nutritional, and microbial factors as diet response predictors for 4 IBS symptoms. Seventy-five IBS patients were randomized to the low FODMAP (n=38) or NICE diet (n=37) for 4 weeks. Baseline measures included stool samples evaluated by the GA-map™ Dysbiosis Test, generating a Dysbiosis Index, 4-day food diaries for the calculation of the average daily energy and FODMAP intake (DIETIST XP V.3.1, Kostdata.se, Sweden), Patient Health Questionnaire and Hospital Anxiety & Depression Scale to measure somatic symptoms and psychological distress, respectively. Outcome measures were 4 subscales (bloating, constipation, diarrhea, and pain) of the Gastrointestinal Symptom Rating Scale treated as continuous variables in linear mixed models.

Models included the main effect of baseline predictors on subscale scores, the main effect of time as a linear slope, and the interaction effect testing if baseline variables predict the response slope. Lastly, a diet variable (including its main effect and all interactions) was added to test if baseline variables differentially predict response to the low FODMAP and NICE diet.

Results: We included 65 patients; 32 on low FODMAP and 33 on NICE diet. In models without covariates, both diets were shown to be effective and reduced the severity of bloating, diarrhea, pain (all p<0.0001), and constipation (p<0.05). Adding the diet variable to the model without covariates indicated absence of differences in response between the diets for any of the symptoms, thereby confirming an earlier analysis of Böhn *et al.* For pain, a lower dysbiosis index (p=0.02) and higher energy intake (p=0.003) predicted better response to both diets.

For constipation, lower dysbiosis index predicted better response to both diets (p=0.009). For diarrhea, FODMAP intake tended to be associated with response to both diets (p=0.057), driven by a significant association between higher baseline FODMAP intake and better response to the NICE diet.

For bloating, higher levels of psychological distress predicted worse response to both diets (p=0.03). FODMAP intake emerged as a differential predictor for treatment response (interaction effect: p=0.04), with higher baseline intake associated with worse response to the low FODMAP diet, and better response to the NICE diet.

Conclusion: Patterns of psychological, nutritional, and microbial factors predict treatment response to the low FODMAP and NICE diet for specific symptoms. These findings may inform individual tailoring of dietary treatment advice in IBS patients.

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P0787

EFFICACY AND SAFETY OF LUVOS HEALING EARTH FOR SYMPTOMS OF FUNCTIONAL DYSPEPSIA AND IRRITABLE BOWEL SYNDROME - RESULTS OF A PROSPECTIVE NON-INTERVENTIONAL STUDY

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Introduction: Functional Dyspepsia and irritable bowel syndrome are common in primary medical care. In self-medication, many patients report a significant improvement in gastrointestinal symptoms by taking Healing Earth. As yet, systematic data on Healing Earth for treating gastrointestinal symptoms in functional GI-Disease are lacking.

Aims & Methods: Effectiveness of Healing Earth (Luvos®) in patients with functional dyspepsia and irritable bowel symptoms. Patients between 18 and 75 years of age with typical symptoms of functional dyspepsia and irritable bowel syndrome without organic correlate in past diagnostics were included in the study. Complaints of at least moderate severity needed to exist for at least 5 days in the previous 2 weeks - there should have been no changes of relevant medication in the last 3 months. Therapy with Luvos® Healing Earth ultrafein was carried out with 3x1 measuring spoons over 6 weeks. The primary target parameter was the validated Nepean Dyspepsia Index (NDI) and an analogously constructed total score for typical irritable bowel syndrome, while the secondary target parameters were quality of life and tolerance.

Results: A total of 64 patients (53% female, mean age 49.5 years) were included in the study; 46 patients were available for per-protocol analysis. The mean NDI at the beginning of the study was 44.3 on average. After 3 weeks of therapy, the NDI value dropped by an average of 5 points (p < 0.04), after 6 weeks of therapy by a further 15 points (p < 0.001); overall, it decreased by 43 percent compared to baseline value. The IBS total score fell from 29.8 to 27.0 after 3 weeks and to 16.2 after 6 weeks (p < 0.001); overall it decreased by 47 percent. With very good tolerance, life quality improved significantly after 6 weeks of therapy.

Conclusion: In the present prospective study, Healing Earth proved to be an effective and well tolerated in patients with functional dyspepsia and irritable bowel syndrome. A clear therapeutic effect is achieved after a therapy duration of more than 3 weeks with further improvement after 6 weeks of treatment.

Disclosure: Nothing to disclose

P0788

A DOUBLE-BLIND, RANDOMIZED PLACEBO-CONTROLLED TRIAL OF EFFICACY AND SAFETY OF THE FOOD SUPPLEMENT, STANDARDIZED FOR MENTHOL, LEMONENE AND GINGEROL, IN PATIENTS WITH IRRITABLE BOWEL SYNDROME AND FUNCTIONAL DYSPEPSIA

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Introduction: Irritable bowel syndrome (IBS) is the most common functional disorder. Moreover, 27-82,6% of patients with IBS also have functional dyspepsia (FD) symptoms. The overlap of these diseases significantly worsens the quality of life, reduces social activity of patients, and also requires significant healthcare expenses for their examination and treatment. The efficiency of the recommended medicines for IBS and FD treatment is low. Considering that almost all components of the IBS pathogenesis are known, we analyzed the effectiveness of the Food Supplement, standardized for menthol, lemonene and gingerol, the components of which affect each pathogenesis stage of functional gastrointestinal disorders.

Aims & Methods: A double-blind, randomized placebo-controlled trial to assess efficacy and safety of the food supplement, standardized for menthol, lemonene and gingerol in IBS and IBS/FD patients was performed. Using a random number generator, the 56 patients with IBS (17 men aged 32.8 [18; 57] years and 21 women aged 33.2 [18; 57] years) and IBS/FD (6 men aged 31.8 [21; 47] years and 12 women aged 33.2 [20; 59] years) were randomly assigned to either the intervention group (IG) - 28 persons or the control placebo group (CG) - 28 persons. There were no statistical significant differences in gender, age, diagnosis and disease duration between the groups.

The non-functional causes for the symptoms were excluded by the evaluation of detailed medical history, physical examination, blood tests, stool analysis, and endoscopy with biopsies. The diarrhea predominant IBS patients and mixed bowel habits IBS patients were treated with smooth muscle antispasmodics. The constipation predominant IBS patients were treated with smooth muscle antispasmodics and laxative. IBS/FD patients were treated with smooth muscle antispasmodics and proton pump inhibitors.

After randomization the IG and the CG patients took 1 capsule of food supplement (peppermint oil (40% menthol, 1.5% limonene) 240 mg; ginger oil (14% gingerol) 50 mg; olive oil 440 mg) or placebo (olive oil 730 mg) once a day in addition to the standard treatment for 30 days. Researchers and patients were not informed who was taking the food supplement or placebo. During the 30 days of the study, 3 outpatient visits were conducted (Visit 1 - 1 day, Visit 2 - 15±2 days and Visit 3 - 30±2 days). At each visit patients were tested with "7x7" questionnaire that allowed them to answer questions concerning the symptoms of IBS and FD, and the physician to objectively evaluate their frequency and intensity, having obtained a quantitative description of their severity. According to the total sum of "7x7" questionnaire points patients were evaluated as: 0-1 points - healthy; 2-6 points - borderline ill; 7-12 points - mildly ill; 13-18 points - moderately ill; 19-24 points - markedly ill; 25 or more - severely ill.

Results: The average total "7x7" of questionnaire points was 13 [9,75; 16] for IG and 15,5 [12,75; 19] for CG (moderately ill) with no significant statistical difference at Visit 1 ($p=0,1$). At the Visit 2 the total points of "7x7" in IG and CG decreased to 8,5 [5; 12,25] and 10 [5; 17,5] points respectively

(mildly ill) with no significant differences between groups ($p = 0,42$). The average total of points of the "7x7" questionnaire at the Visit 3 in IG was significantly lower than CG: 6 [2,75; 9,5] points (borderline ill) and 9 [6,75; 16,25] points (mildly ill) respectively ($p = 0,02$).

Conclusion: Standardized for menthol, lemonene and gingerol food supplement increases the effectiveness of therapy in IBS and FD patients.

Disclosure: Nothing to disclose

P0789

EFFICACY OF RIFAXIMIN ON BLOATING IN PATIENTS WITH DIARRHOEA-PREDOMINANT IRRITABLE BOWEL SYNDROME: A POOLED ANALYSIS OF THREE PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED TRIALS

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Introduction: Bloating is common in patients with irritable bowel syndrome (IBS). Two-week course(s) of rifaximin have been shown to significantly improve IBS with diarrhoea (IBS-D) symptoms compared with placebo. Rifaximin is indicated in the United States and Canada for the treatment of adults with IBS-D.

Aims & Methods: The aim of the current post hoc analysis of three phase 3 trials was to further examine the efficacy of rifaximin in improving bloating. Adults with IBS-D were randomly assigned to receive double-blind rifaximin 550 mg three times daily or placebo for 2 weeks, followed by a 4-week treatment-free follow-up period to evaluate response. In Trials 1 and 2, bloating severity was determined by patient response to a daily question, "In regards to your specific IBS symptom of bloating: on a scale of 0-6, how bothersome was your IBS-related bloating today?" and patient response to a weekly question, "In regards to your IBS symptom of bloating, compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS symptom of bloating?" Patients rated symptoms on a scale of 0 (not at all) to 6 (a very great deal). In Trial 3, bloating severity was determined by patient response to the question, "In regards to your specific IBS symptom of bloating, on a scale of 0-6, how bothersome was your IBS-related bloating in the last 24 hours?" Bloating responders were defined in 2 ways in this analysis: patients achieving either a ≥ 1 - or ≥ 2 -point decrease (improvement) from baseline in weekly average bloating score for ≥ 2 weeks of the first 4 weeks post-treatment. Durable response was defined as maintenance of this bloating response for each week of an additional 6 weeks of follow-up (through week 10 post-treatment). *P* values were obtained from Cochran-Mantel-Haenszel method, with adjustment for analysis center.

Results: 1894 patients with IBS-D were included in the analysis: rifaximin ($n=952$) and placebo ($n=942$). Overall, the majority of patients were female (71.3%), with a mean age of 46.2 years. At baseline, both the rifaximin and placebo treatment groups had a weekly average bloating score of 3.4. A significantly greater percentage of patients receiving rifaximin were bloating responders versus placebo when response was defined as either a ≥ 1 -point decrease (47.8% vs 38.6%, respectively; $P<0.0001$) or a ≥ 2 -point decrease (23.3% vs 17.8%, respectively; $P=0.003$) in weekly average bloating score for ≥ 2 weeks of the first 4 weeks post-treatment. Least-squares mean change from baseline in bloating scores significantly favoured rifaximin versus placebo at week 1 ($P=0.0497$) and week 2 ($P=0.002$) of treat-

ment and week 1 through week 10 post-treatment ($P \leq 0.01$). Furthermore, durable bloating response was achieved by a significantly greater percentage of patients receiving rifaximin versus placebo for both ≥ 1 -point responders (36.4% vs 28.9%, respectively; $P < 0.001$) and ≥ 2 -point responders (16.1% vs 12.3%; $P = 0.02$).

Conclusion: Rifaximin 550 mg three times daily for 2 weeks provided significant and durable improvement in bloating versus placebo in adults with IBS-D.

References: N/A

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P0790

INFLAMMATORY STATUS IN POST-INFECTIOUS IRRITABLE BOWEL SYNDROME AT TIME OF FECAL MICROBIOTA TRANSPLANTATION AND FOLLOW-UP

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Introduction: Acute gastroenteritis is sometimes followed by post-infectious irritable bowel syndrome (PI-IBS). It is thought that pro-inflammatory signals from preceding infection drives increased gut permeability, which in turn drives chronic gut disturbances, culminating in PI-IBS. Inflammatory status of PI-IBS patients was examined before and 1-3 months after treatment of their PI-IBS with fecal microbiota transplantation (FMT).

That pro-inflammatory cytokines could be elevated in PI-IBS raised a question of whether elevated endotoxins might be present and detectable in peripheral blood to explain this.

Aims & Methods: Identify differences from healthy controls in plasma endotoxin levels and inflammatory biomarkers in PI-IBS patients at time of FMT and 1-3 months follow-up.

Study subjects: Plasma prepared from peripheral blood (median cubital vein) from 50 PI-IBS patients immediately prior to FMT and 36 patients 1-3 months post-FMT follow-up were studied. Data was compared to 104 healthy controls.

The following 39 inflammatory biomarkers were measured (Meso Scale Discovery, cat# K15209D-2): CRP, Eotaxin, Eotaxin-3, FGF(basic), Flt-1, GM-CSF, ICAM-1, IFN- γ , IL-1 α , IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12/IL-23p40, IL-12p70, IL-13, IL-15, IL-16, IL-17A, IP-10, MCP-1, MCP-4, MDC, MIP-1 α , MIP-1 β , PlGF, SAA, TARC, TNF- α , TNF- β , Tie-2, VCAM-1, VEGF, VEGF-C, VEGF-D. Pro-inflammatory capacity of endogenous molecules (e.g., endotoxins) was determined using HEK-TLR4 cells expressing human TLR4 (Invivogen, cat# hkb-htlr4), which release secreted embryonic alkaline phosphatase (SEAP) in response to TLR4 activation. E coli lipopolysaccharide (LPS) was used as standard. SEAP release was measured by conversion of para-nitrophenyl-phosphate to para-nitrophenol (absorbance 405 nm). TLR4 activation equivalent to 3 mEU/ml LPS (lowest concentration able to activate TLR4) or higher plasma concentration was defined as detectable. Wilcoxon signed-rank test was used for statistics.

Results: The following differed at pre-FMT ($p < 0.001$) relative controls (fold change): FGF-basic (0.2, i.e., lower than controls by 5-fold), IL-4 (10), IL-12p70 (2), TARC (0.3), VEGF-D (3). These also differed at follow-up from controls: FGF-basic (0.3), IL-4 (20), IL-12p70 (2), TARC (0.3), VEGF-D (2.5). IL-2 declined at follow-up relative pre-FMT (0.4-fold, $p < 0.005$). PI-IBS patients showed detectable TLR4 activation, if anything, less frequently than healthy controls at pre-FMT (32% vs 48%) and at follow-up (17% vs 48%). Less than 15% of those with detectable activity reached that of a 13 mEU/ml LPS standard. These differences did not reach significance.

Conclusion: Endogenous activators of TLR4 are not usually present in plasma from PI-IBS patients at the time of FMT at levels sufficient to activate TLR4. Activators either fail to pass the gut mucosal barrier or are quickly removed by the liver. Whichever is the case, at the time of receiving FMT for PI-IBS, these patients harbor common immunological abnormalities across a spectrum of inflammatory biomarkers, all of which are functionally connected to T-cell differentiation and TH1/TH2 shifting. It is noteworthy that this was unchanged as of the 1-3 months follow-up.

Disclosure: Nothing to disclose

P0791

FECAL MICROBIOTA TRANSPLANTATION FOR MODERATE TO SEVERE IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is a heterogeneous disorder, and gut dysbiosis may play an important role in its pathogenesis. Treatment modulating gut microbiota has been proposed as a therapeutic option for IBS. Recent observational studies of fecal microbiota transplantation (FMT) have been promising, while randomized controlled trials showed conflicting results. The aim of this study was to evaluate the effectiveness and safety of frozen FMT for the treatment of IBS.

Aims & Methods: This study was a single-arm, open label. Eligible patients were diagnosed according to Rome IV criteria. Severity was evaluated with IBS Symptom Severity Score (IBS-SSS) and IBS-specific quality of life (IBS-QoL). The qualified material for FMT was obtained from 6 healthy, well characterized donors, frozen and administered via colonoscopy. Additional FMT was performed via upper endoscopy or colonoscopy if patient had no response. The primary outcome was a decrease in IBS symptoms at 1 month after FMT. A response was defined as reduction of 50 or more points in IBS-SSS.

Results: A total of 12 patients (7 diarrhea predominant IBS (IBS-D), 4 constipation predominant IBS (IBS-C), 1 mixed type IBS) were enrolled. Frozen FMT was well tolerated. Adverse events were mild and transient. No serious adverse event occurred. Six patients with IBS-D (85.7%) and a patient with IBS-C (25%) had a clinical response and improved IBS-QoL. Four patients who had no response in 1st FMT achieved a clinical response after 2nd FMT (2 via upper endoscopy, 2 via colonoscopy). Seven patients who showed a clinical response had received frozen inoculum from 3 donors, while 4 patients without clinical response from another 3 donors.

Conclusion: FMT is a safe and may be an effective treatment for patients with moderate to severe IBS, especially IBS-D. Second FMT could provide additional clinical improvement for patient without response after first FMT. However, its effectiveness and safety for IBS require larger studies with appropriate placebo groups and which consider recipient and donor factors.

Disclosure: Nothing to disclose

P0792

SYSTEMATIC REVIEW WITH META-ANALYSIS OF LUBIPROSTONE FOR PATIENTS WITH CONSTIPATION

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Introduction: Lubiprostone is a type 2 chloride channel activator that acts increasing the secretion of chloride-rich intestinal fluid and accelerates colonic transit. Since its first clinical data, lubiprostone efficacy and safety have been addressed in clinical trials enrolling patients with chronic idiopathic constipation (CIC), irritable bowel syndrome with predominant constipation (IBS-C) and opioid-induced constipation (OIC), as well as colonoscopy preparation and leaky gut.

Aims & Methods: To systematically review randomized clinical trials (RCTs) assessing efficacy of lubiprostone for patients with CIC, IBS-C and OIC. Searches were conducted in PubMed, LILACS, Cochrane Collaboration Database, and Centre for Reviews and Dissemination. Lubiprostone RCTs reporting outcomes of spontaneous bowel movements (SBM) and abdominal pain or discomfort were deemed eligible. Meta-analysis was performed calculating risk ratios and 95% confidence intervals.

Results: Searches yielded 109 records representing 93 non-duplicate publications, and 11 RCTs (involving 978 CIC, 1,366 IBS-C, 1,300 OIC, total=3,644 patients) met inclusion criteria. Among CIC studies, lubiprostone was significantly superior to placebo for all SBM-related outcomes except for full responder rate in one study. Lubiprostone demonstrated a better efficacy profile in follow-up durations ranging from 1 to 8 weeks. In terms of abdominal discomfort endpoints, lubiprostone-treated patients had significantly lower scores 4 weeks after treatment initiation in one study, but two other studies did not observe a statistically significant difference. In the CIC meta-analysis, lubiprostone increased the likelihood of a patient achieve a full-responder status by 1.67 (95% CI 1.36-2.06) and present a SBM in 24 hours of 1.90 (1.56-2.31). In the IBS-C studies, all selected SBM-related outcomes were significantly better among lubiprostone patients, even in longer follow-ups (up to 3 months). For abdominal pain measures, 3 RCTs assessed mean scores in 1, 2 and 3 months after treatment initiation. Johanson et al. observed a higher mean improvement from baseline in abdominal pain score after 1 and 2 months of lubiprostone therapy. Patients enrolled in the Drossman et al. trial presented better improvement in abdominal pain after 2 and 3 months of lubiprostone as compared to patients receiving placebo. Findings from OIC RCTs were less consistent for each of the selected outcomes. Statistically significant differences in favor of lubiprostone were seen in some of the included studies for mean change from baseline in SBM frequency at week 8-12 and overall; SBM within 24 hours; overall responder rate; median time to first SBM; and mean improvement in abdominal discomfort scales. Meta-analysis was feasible for SBM within 24 hours rate only (without statistical significance).

Lembo et al. conducted a multicenter trial that enrolled 248 patients with CIC to receive lubiprostone for 48 weeks. Overall, lubiprostone significantly improved constipation severity, abdominal bloating, and abdominal discomfort when compared to baseline ($p < 0.0001$).

Additionally, lubiprostone has demonstrated a favorable safety profile in RCTs, pooled analysis and meta-analysis of both RCTs and extension studies. The most common adverse events were mild to moderate nausea and diarrhea.

Conclusion: Our findings demonstrated that lubiprostone is superior to placebo in terms of SBM frequency for CIC, IBS-C and OIC. In terms of abdominal symptoms, the most pronounced effect was seen for abdominal pain in IBS-C patients.

Disclosure: Maria do Carmo Friche Passos has served as Global Advisory Board Member for Takeda, Speaker for EMS, Ache, Mantecorp. Gabriel Cyrillo Corradino is an employee of Takeda Pharmaceuticals Brazil (Clinical Research Analyst) Luciana Guedes is an employee of Takeda Pharmaceuticals Brazil (Sr Medical Manager for Gastroenterology).

P0793

A NOVEL SCORE TO EVALUATE ABDOMINAL SYMPTOM IMPROVEMENT IN PATIENTS WITH CONSTIPATION-PREDOMINANT IBS DEMONSTRATES EFFICACY OF LINACLOTIDE FOR IMPROVING ABDOMINAL BLOATING, DISCOMFORT, AND PAIN IN A PHASE 3B TRIAL

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Introduction: The Diary for Irritable Bowel Syndrome Symptoms-Constipation (DIBSS-C) is a new patient-reported outcome (PRO) measure of bowel and abdominal symptoms developed by the IBS Working Group of the Critical Path Institute's Consortium for use in IBS-C trials. A multi-item abdominal score (AS) was derived from the 3 abdominal symptom items of the DIBSS-C (abdominal bloating, abdominal discomfort, and abdominal pain).

Aims & Methods: Linaclotide is a GC-C agonist approved for treating IBS-C as well as chronic idiopathic constipation. This is the first randomized, double-blind, phase 3B study to evaluate the efficacy of linaclotide vs placebo for treating IBS-C using the new AS for assessing abdominal symptom severity.

IBS-C patients with baseline abdominal pain ≥ 3 (0-10 scale) were randomized to linaclotide 290 mg or placebo daily for 12 weeks, followed by a 4-week randomized withdrawal period (RWP). The weekly AS (0-10 scale, higher number indicates worse symptoms) is based on the average of daily abdominal bloating, discomfort, and pain (0=None to 10=Worst possible). The primary endpoint was overall change from baseline (CFB) in AS, analyzed at each week over 12 weeks, using a mixed model with repeated measures (MMRM). Secondary endpoints were CFB in 12-week AS evaluated using cumulative distribution function (CDF) and 6/12 week AS responder (AS improvement ≥ 2 points for $\geq 6/12$ weeks). Primary and secondary endpoints were controlled for multiplicity. Additional endpoints included CFB in individual abdominal symptoms. Adverse events (AEs) were monitored throughout.

Results: 614 patients (mean age 46.7 yrs; 81% female) were randomized. Overall AS improvement was significantly greater for linaclotide vs placebo (mean CFB -1.9 vs -1.2; $p < 0.0001$). AS improvement for linaclotide vs placebo was significant from Week 1 onward ($p \leq 0.0002$). CDF curves show improvement in 12-week AS for linaclotide with significant separation from placebo ($p < 0.0001$). Linaclotide 6/12 week AS responder rate was 40.5% vs 23.4% for placebo (odds ratio=2.2 [95% CI 1.55, 3.12; $p < 0.0001$]). Individual abdominal symptoms similarly improved with linaclotide. Diarrhea was the most common treatment-emergent AE (linaclotide=4.6%, placebo=1.6%). Symptoms did not worsen relative to baseline in the RWP.

Conclusion: Linaclotide significantly improved multiple abdominal symptoms important to IBS-C patients (abdominal bloating, discomfort, and pain) compared with placebo, as measured by a novel, multi-item abdominal score. The AS, derived from the abdominal symptom items in the DIBSS-C, should be used in future IBS-C clinical studies to measure clinically meaningful improvements in these three abdominal symptoms in IBS.

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P0794 WITHDRAWN

P0795 WITHDRAWN

P0796

LINACLOTIDE SAFETY AND EFFICACY IN CHILDREN AGED 7 TO 17 YEARS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION

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Introduction: Irritable bowel syndrome with constipation (IBS-C) is a disorder commonly seen by pediatric gastroenterologists. There are currently no approved therapies for IBS-C in children.

Aims & Methods: This is the first study evaluating the safety and efficacy of linaclotide (LIN) for the treatment of IBS-C in children aged 7-17 years. This was a multicenter, randomized, double-blind, placebo (PBO)-controlled, parallel-group, safety and efficacy dose finding study of a range of LIN doses compared to PBO. Participants who met Rome III criteria for child/adolescent IBS were randomized to once-daily PBO or LIN doses for 4 weeks. Those aged 7-11 years were randomized to 18-145 µg (based on weight) and those aged 12-17 years were randomized to 36-290 µg. The primary efficacy endpoint was change from baseline in overall spontaneous bowel movement (SBM) frequency rate. Secondary efficacy endpoints included change from baseline in daytime abdominal pain and bloating, stool consistency, straining severity, and overall complete SBM (CSBM)

frequency rate. Descriptive statistics are provided for efficacy parameters. Safety assessments included adverse events (AEs), AEs of special interest (AESIs), treatment-emergent AEs (TEAEs), causality, severity, and serious AEs.

Results: 101 participants were randomized; 41 were aged 7-11 years and 60 were aged 12-17 years. A numerical trend toward greater efficacy was observed with increasing LIN dose vs. PBO for the primary endpoint (change from baseline in SBM frequency rate), as well as straining severity, stool consistency, and CSBM frequency rate in the ITT population). An exploratory dose with a limited sample size, the LIN 290 µg group demonstrated numerically greater improvement in abdominal pain compared to PBO, a trend not observed in the other LIN doses. TEAEs were reported in 38% (LIN A; n=11), 29% (LIN B; n=6), 25% (LIN C; n=6), 13% (LIN 290 µg; n=1), and 16% (PBO; n=3) of participants. The most commonly reported TEAEs (occurring in ≥5% of participants in any LIN group) were diarrhea, abdominal pain, and vomiting. No AESIs, SAEs of diarrhea, or deaths were reported. In the 7-11 year age group, no treatment-related TEAEs, SAEs, or AEs leading to discontinuation were reported. In the 12-17 year age group, two SAEs were reported (fecaloma post LIN 36 µg treatment; anaphylactic reaction with PBO) and two participants reported AEs leading to discontinuation (anaphylactic reaction [reported above] and hematemesis with PBO [n=1]; diarrhea with LIN 72 µg [n=1]).

Conclusion: LIN appeared to be safe and well tolerated at daily doses up to 145 and 290 µg in patients with IBS-C aged 7-11 and 12-17 years, respectively. A numerical trend toward greater efficacy was observed with increasing LIN doses vs. PBO for the primary endpoint and secondary endpoints related to bowel habits.

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P0797

RIFAXIMIN IS EFFICACIOUS FOR THE TREATMENT OF IRRITABLE BOWEL SYNDROME WITH DIARRHOEA IN ADULTS PREVIOUSLY TREATED WITH OTHER IBS MEDICATIONS

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Introduction: Antidiarrheals and antispasmodics are frequently used to manage irritable bowel syndrome (IBS) symptoms but only target select symptoms. Rifaximin is indicated in the United States and Canada for the treatment of adults with IBS with diarrhoea (IBS-D) and improves multiple IBS symptoms, including the composite endpoint of abdominal pain and stool consistency. Data regarding rifaximin efficacy after nonresponse to other IBS-D medications are limited.

Aims & Methods: The aim was to assess efficacy of two 2-week courses of rifaximin for IBS-D in adults who previously tried other IBS medications. In a phase 3, randomized, double-blind, placebo-controlled trial (TARGET 3), adults with IBS-D received 2 weeks of open-label rifaximin 550 mg TID. Patients with a composite response (weekly response for abdominal pain [$\geq 30\%$ decrease from baseline in mean weekly pain score] and stool consistency [$\geq 50\%$ decrease from baseline in days/week with Bristol Stool Scale type 6/7 stool] during ≥ 2 of the first 4 weeks post-treatment) who had symptom recurrence during an 18-week observation phase were randomized to receive a repeat 2-week treatment with rifaximin 550 mg TID or placebo. Composite response, response to individual composite endpoint components, and bloating response (≥ 1 -point decrease from baseline in weekly mean score during ≥ 2 of the first 4 weeks post-treatment) were assessed. This post hoc analysis evaluated the subgroup of patients with a history of IBS medication use before the study.

Results: In the open-label population (n=2579), the most common prior IBS medications were loperamide (22.6%), dicyclomine (10.4%), bismuth subsalicylate (8.1%), and hyoscyamine (6.8%). Overall, 1258 patients (48.8%) had taken IBS medications prior to study entry and were included in the OL efficacy analysis. In the open-label phase, 48.6% of 1258 patients with prior IBS medication use were rifaximin responders for abdominal pain plus stool consistency. Response rates for abdominal pain, stool consistency, and bloating were 61.4%, 62.2%, and 60.3% respectively. In the double-blind, repeat-treatment phase (rifaximin, n=185 [72.4% female; mean, 6.8 y since diagnosis]; placebo, n=185 [71.4% female; mean, 5.1 y since diagnosis]), the percentage of responders with prior IBS medication use was significantly greater with rifaximin vs placebo for the composite endpoint (40.0% vs 23.2%; $P < 0.001$), individual components of composite endpoint (abdominal pain: 60.0% vs 40.5%; $P < 0.001$; stool consistency: 50.3% vs 34.6%; $P = 0.002$), and bloating (53.5% vs 40.5%; $P = 0.01$).

Conclusion: Two-week courses of rifaximin were efficacious in improving abdominal pain, stool consistency, and bloating in adults with prior IBS medication use. Thus, rifaximin can be used in patients unresponsive to other IBS-D therapies.

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P0798

LOW FODMAP DIET FOR IRRITABLE BOWEL SYNDROME: SOME ANSWERS TO THE DOUBTS FROM A LONG-TERM FOLLOW-UP

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Introduction: The Low FODMAP diet (LFD) is a possible therapy for irritable bowel syndrome (IBS). It is based on the exclusion of foods containing fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) and consists in a first phase of strict restriction, followed by a gradual reintroduction of the individual categories of FODMAPs according to individual tolerance. This enables the personalization of the diet and its use in the long term (Adapted Low FODMAP Diet, AdLFD). The present study investigated the short and long-term efficacy and nutritional adequacy of the LFD and the patients' long-term acceptability. Adherence to the diet, both in the short and long-term, and patients' ability to identify foods triggering their digestive symptoms were also assessed.

Aims & Methods: Under the guidance of a skilled nutritionist, 73 IBS patients received a LFD (T0) and after 2 months (T1) 68 started the reintroduction phase. At the end of this period (T2) 59 were advised to go on an AdLFD and 41 were evaluated again after a 6-24 month (12.7 ± 10.0) follow up (T3). At each time there was an evaluation of IBS symptoms (IBS-SSS), bowel habits (VAS), quality of life (SF-36), anxiety and depression (HADS), adherence to the diet (FARS) and its acceptability, degree of symptom improvement and of satisfaction with the diet. Bioelectrical Impedance Analysis (BIVA) and anthropometric measurements were also carried out to evaluate any changes in body composition.

Results: The LFD improved IBS-SSS (total score $p < 0.001$; single items $p < 0.001$, except for bowel habit dissatisfaction $p < 0.05$) and bowel habits (watery stools, defecatory urgency, abdominal pain and bloating $p < 0.05$), both in the short (T1) and long-term (T3), in comparison with the T0. The LFD was also effective in improving quality of life (both physical and mental indexes) and anxiety and depression at T1 and T3 in comparison with the T0 ($p < 0.001$ and $p < 0.05$, respectively), even if adherence decreased (T1: 23.1 ± 2.4 vs. T3: 23.1 ± 2.4 ; $p < 0.001$). Degree of symptom relief (1.5 ± 0.9 at T1 and 1.2 ± 1.3 at T3) and of satisfaction with the diet (8.5 ± 1.3 at T1 and 8.0 ± 1.9 at T3) were constantly high. The LFD did not affect nutritional adequacy, as shown by unchanged BIVA and anthropometrical parameters both at T1 and T3. Patients complain of spending more time and money on shopping and having greater difficulty eating out, but they reported a better relationship with meals and a more positive approach to food. The perception of trigger foods was found to be quite different, especially regarding polyols, fructose and galactans ($k < 0.2$), between T0 and T2.

Conclusion: Even if some problems of acceptability and adherence were reported, the LFD was effective in improving IBS symptoms, anxiety, depression and quality of life also in the long-term without affecting nutritional adequacy. The LFD improved patients' relationship with food and the degree of symptom relief and satisfaction with the diet were striking. The reliability of the patients' judgment in detecting the real FODMAP foods able to provoke their symptoms was not high; it underlines the pivotal role of a skilled nutritionist in the management of this kind of diet.

Disclosure: Nothing to disclose

P0799 WITHDRAWN

P0800 WITHDRAWN

P0801

THE ASSOCIATION BETWEEN PROTON PUMP INHIBITORS AND COLONIC DIVERTICULITIS

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Introduction: Colonic diverticular disease, especially diverticulitis constitutes a major cause of hospitalization and an economic burden in developed countries. Proton pump inhibitors (PPIs) are among the commonest drugs used. Several studies have reported that PPIs use caused dysbiosis.

Aims & Methods: We aimed to explore whether PPI use is associated with diverticulitis and to investigate whether PPIs use affects the severity of diverticulitis. A retrospective study of patients who were hospitalized with documented diverticulitis during a 10 years period were enrolled in the study with a cross-matched control group of patients for age and gender with diverticulosis but without diverticulitis.

Results: Overall 300 patients with confirmed endoscopic diagnosis of diverticulosis were included in the study, of them 115 had an at least one episode of diverticulitis during the first year after diagnosis of diverticulosis (group A), compared to 185 patients who didn't develop diverticulitis (group B). The average age in groups A and B was 71 ± 6.9 vs. 70.6 ± 7.7 years, respectively ($P=0.3$). Male gender was almost similar in the two groups (73% for group A vs. 68% for group B, $P=0.1$). Notably, PPI use was significantly associated with the development of acute diverticulitis among patients with diverticulosis (OR 48.364, 95% CI 22.85-102.38, $P<0.0001$), while non-steroidal anti-inflammatory drugs use wasn't associated with the development of diverticulitis (OR 1.1, 95% CI 0.527-2.35, $P=0.7$). PPI use didn't not affect the severity of the diverticulosis as assessed by Hinchey classification which was 1.5 ± 0.7 for group A vs. 1.6 ± 0.7 for group B ($P=0.3$). Moreover, there was a trend for higher diverticulitis episodes during the first year following diverticulosis diagnosis (1.7 ± 0.8 vs. 1.3 ± 0.5 episode/patient) for groups A and B, respectively ($P=0.08$).

Conclusion: PPI use was significantly associated with diverticulitis episodes among patients with diverticulosis. PPI therapy should be considered carefully and discontinued once there are no definite indication in patients with diverticulosis.

Disclosure: Nothing to disclose

P0802

ALTERED GUT MICROBIOTA IS NOT ASSOCIATED WITH DIVERTICULOSIS NOR PREDICTIVE OF FUTURE DIVERTICULITIS IN A POPULATION-BASED COLONOSCOPY STUDY

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Introduction: The aetiopathogenesis of diverticular disease is unknown and studies on the gut microbiome have shown divergent results¹. Many studies have been conducted on symptomatic patients at endoscopy or those in tertiary care.

Aims & Methods: We aimed to study the faecal and mucosa-associated microbiome in a population-based colonoscopy study of control subjects, those with diverticulosis and follow up of individuals that later developed diverticulitis.

The PopCol study, conducted in Stockholm, Sweden, recruited a random sample of 3556 adults of which 745 underwent colonoscopy and has been previously described in detail². Overall, 130 subjects (17.5%) had diverticulosis³, not associated with mucosal or serological inflammation⁴. 16S rRNA gene sequencing was conducted on available sigmoid biopsy samples from 376 individuals

(83 with diverticulosis) and available faecal samples from 185 individuals (37 with diverticulosis), 144 individuals had both faeces and biopsies available. Using the Stockholm VAL-database health registry and electronic chart review from in- and out-patient visits we identified individuals who subsequently developed diverticulitis up to 13 years after sample collection, 14 with biopsy samples and 8 with faecal samples. In a case-control design matching for gender, age (± 5 years), smoking and antibiotic usage, we compared taxonomic composition, richness and diversity of the microbiome between those with or without diverticulosis, and between those who developed diverticulitis versus those that did not.

Results: No differences in microbiome richness or diversity were observed for subjects with or without diverticulosis, nor for those that developed diverticulitis and those that didn't, in either sample type (table 1). No bacterial taxa were significantly associated with diverticular disease when adjusting for age, gender and smoking status.

Conclusion: In a population-based cohort no distinct microbial signature was observed in diverticulosis or in individuals that later develop diverticulitis, suggesting no, or limited, role for the gut microbiota in the aetiopathogenesis of diverticular disease.

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	Richness	Shannon Diversity
Diverticulosis Samples		
Biopsy (n)	83	83
Case average	548	4.00
Control average	558	4.05
P	0.647	0.408
Fecal (n)		
Case average	536	3.80
Control average	571	3.98
P	0.278	0.146
Diverticulitis samples		
Biopsy (n)	14	14
Case average	483	3.84
Control average	541	3.99
P	0.218	0.372
Fecal (n)		
Case average	479	3.68
Control average	554	3.98
P	0.132	0.069

[Table. Chao1 richness and Shannon's diversity.]

P0803

CLINICAL COURSE AND OUTCOMES OF ACUTE DIVERTICULITIS AMONG ISRAELI POPULATION, DOES ETHNICITY MATTER?

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Introduction: Acute diverticulitis is considered as the leading and most burdensome complication of colonic diverticulosis. However, risk factors for its development and predictors of its course are still poorly defined. Importantly, little research has addressed the effect of ethnicity on the course of diverticulitis.

Aims & Methods: The current study aims to evaluate the impact of ethnicity on diverticulitis course and outcomes in the diverse and unique ethnic landscape of Israel. We performed a retrospective review of the charts of patients with a radiologically confirmed, first episode of acute diverticulitis. Patients were then divided, based on identity details and national databases, into religious ethnicity of two main groups, Arabs and Jews, as well as into Jewish subgroups. Patients outcomes and disease course including hospitalization duration, complications (abscess, perforation, fistula, obstruction) and recurrent episodes of diverticulitis were documented and compared among the different ethnic populations.

Results: Overall, 637 patients were hospitalized with a radiologically confirmed first episode of diverticulitis between the years 2004-2017. The

Arab population were more likely to have a first episode of acute diverticulitis at a younger age compared to their Jewish counterparts (51.8 vs. 59.4 years, $P < 0.001$), respectively. Complicated course (16% vs. 15%; $P = 0.08$) as well as relapsing episode rates (33% vs. 38%; $P = 0.36$) didn't differ significantly between both groups. Likewise, independent association between ethnicity group and increased risk of complications was not evident in a multivariate analysis. Jewish subgroup analysis revealed varied age and gender at presentation between Ashkenazi and Sephardic groups. Yet, complications (39.4% vs. 37.6%; $P = 0.69$) as well as recurrent diverticulitis rates (14.7% vs. 16.7%; $P = 0.6$) were comparable. Analysis according to the place of birth showed that patients born in Asia/middle east (8.5% vs 17.8%; $P = 0.09$) and North Africa (7.4% vs. 17.8%; $P = 0.07$) had prominently decreased rate of complications compared to those born in Israel, but this was only close to significance.

Conclusion: Varied by age and gender at presentation with acute diverticulitis, patients within different ethnic groups had generally a similar complications rate and disease course.

Disclosure: Nothing to disclose

P0804

FECAL CALPROTECTIN EXPRESSION CORRELATES WITH THE SEVERITY OF THE "DICA" SCORE IN PATIENTS WITH ENDOSCOPIC DIAGNOSIS OF DIVERTICULOSIS/DIVERTICULAR DISEASE

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Introduction: The recent endoscopic classification called "DICA" (Diverticular Inflammation and Complication Assessment) has showed a significant relationship between severity of DICA score and clinical and demographic characteristics of people having diverticulosis/diverticular disease.

Aims & Methods: Aim of this study was to assess whether there was a relationship between the fecal calprotectin (FC) expression and the severity of DICA score.

FC was available at baseline of 904 prospective patients at the first diagnosis of diverticulosis/diverticular disease, and classified according to DICA classification. It was collected three days after the colonoscopy.

Results: The study group consisted of 904 patients (443, 49.0% males and 461, 51.0% females). According to DICA classification the study group was subdivided in 524 (58.0%) DICA 1 patients, 277 (30.6) DICA 2 patients, and 103 (11.4%) DICA 3 patients. In 710 (78.5%) patients abdominal pain was present.

Mean (IQR) FC value was 41.9 (12-52) $\mu\text{g/dL}$ in DICA 1, 71.4 (12-87) $\mu\text{g/dL}$ in DICA 2, and 95.7 (23-153) $\mu\text{g/dL}$ in DICA 3 ($p < 0.000$, Kruskal-Wallis test). In DICA 1 group, mean (IQR) FC value was 52.5 (12-58) $\mu\text{g/dL}$ in symptomatic patients and 17.6 (12-42) $\mu\text{g/dL}$ in asymptomatic patients ($p < 0.000$, Kruskal-Wallis test). In DICA 2 group, mean (IQR) FC value was 74.4 (18-88) $\mu\text{g/dL}$ in symptomatic patients and 34.4 (12-24) $\mu\text{g/dL}$ in asymptomatic patients ($p < 0.000$). In DICA 3 group there was no asymptomatic patient.

Conclusion: This prospective study seems to confirm that FC is linked to the severity of DICA score, and a clear cut-off seems also able to differentiate symptomatic from asymptomatic patients.

Disclosure: Nothing to disclose

P0805

THE RATE OF ADVANCED COLONIC NEOPLASIA DIDN'T DIFFER AMONG PATIENTS AFTER ACUTE DIVERTICULITIS COMPARED TO AVERAGE RISK CONTROLS; A STUDY ON 1852 PATIENTS

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Introduction: The average rate of colorectal cancer in diverticulosis patients along with recent reports doubting the benefit of prompt colonoscopy after acute episode of diverticulitis mandates further evaluation of colonoscopy yield and timing in this regard.

Aims & Methods: The current study aims to determine whether the rate of advanced colonic neoplasia after acute diverticulitis differs from that of average risk patients, and to identify risk factors associated with their development. In this retrospective study, all patients hospitalized to surgery ward in the years 2008-2016 with radiographically confirmed acute diverticulitis who completed colonoscopies within 1 year of index hospitalization were included. Patients referred for screening colonoscopy in the same years were included as a control group. We compared the rate of colorectal cancer and advanced polyp diagnosis rates between both groups before and after adjustment for age, sex and colonoscopy preparation quality. Moreover, we investigated risk factors associated with increased rate of advanced neoplasia diagnosis.

Results: 350 patients were included in the diverticulitis group and 1502 patients in the screening colonoscopy control group. Colorectal cancer diagnosis rate (1.7% vs. 0.3%; $p=0.09$) as well as overall diagnosis rate of advanced neoplasia (12.3% vs. 9.6%; $p=0.19$) were not significantly different when comparing findings from AD and control groups, respectively. Complicated diverticulitis course, however, was associated with increased risk of advanced neoplasia diagnosis (OR 3.729, 95% CI 1.803-7.713; $P=0.01$).

Conclusion: The rate of advanced neoplasia diagnosis after acute diverticulitis didn't differ from that of average risk population. Complicated course, however, was a potential risk factor.

Disclosure: Nothing to disclose

P0806

GENETIC MARKERS IN DIVERTICULOSIS AND DIVERTICULAR DISEASE - EXPERIENCES FROM GENETIC TESTING IN THE BULGARIAN POPULATION

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Introduction: Diverticulosis is an anatomical structural change in the intestinal wall and usually presents asymptotically. It can progress to diverticular disease, in about 20% of the cases; of which 15% will develop complications. Connelly T. et al. was the first to show a genetic association between the genetic single nucleotide polymorphism rs7848647 in the TNFSF15 gene and the risk for surgical diverticulitis (1).

Aims & Methods: The aims of this study are to examine the risk allele of

rs7848647 in patients with diverticulosis and diverticular disease (with and without complications) and to compare them to a control group of healthy patients.

For the first time in Bulgaria we examine the genetic role of this SNP in the TNFSF15 gene and we compare the obtained genetic data for both patients and controls to the general population and the populations in Europe, the United States and Africa (2).

54 patients (mean age 67 ± 12) were randomly selected from a group of 453 with diverticulosis and diverticular disease, who were followed for a period of 5 years (2013-2018) in City Clinic Gastroenterology. Genotyping was performed in IMDL "Genome Centre Bulgaria". DNA was isolated using ethanol precipitation and SNP genotyping was performed by Sanger sequencing, targeting the promotor region of the TNFSF15 gene, where rs7848647 is located. This is a pilot study for the Bulgarian population.

Results: In the examined cohort of 54 patients, 3 of them were homozygous carriers of the A allele (5%), 23 were heterozygous A/G carriers (43%) and 28 were homozygous carriers of the G allele (52%). Of them, 35 are female and 19 are male. Genotype distribution of the risk allele G among patients with diverticulosis showed that 5 were homozygous carriers of the G/G genotype and 5 were heterozygous A/G carriers. The rest of the patients had diverticular disease, of which 6 presented with acute diverticulitis and 38 with chronic diverticulitis.

3 of the patients with acute diverticulitis underwent surgical treatment, all of which were heterozygous A/G for the targeted SNP. Eight of the chronic diverticulitis patients underwent surgical treatment; 3 of them were heterozygous A/G carriers and 5 were homozygous G/G carriers. In all cases requiring surgical treatment the patients carried at least one G allele.

In the tested cohort, 51 patients were carriers of the G allele. Of them, 10 presented with diverticulosis and 41 with diverticulitis, of which a total of 11 required surgical intervention. The remaining 30 were treated conservatively, 3 of which presented with acute diverticulitis and 27 with chronic diverticulitis. Statistical analysis showed that even though the G allele had the major frequency, there was no statistically significant association between the previously reported risk allele and the need for operative treatment. Genotype proportions were analogous to data from the European population, showing no statistical difference.

Conclusion: Considering that the groups used in the first study of rs7847647 by Connelly et al., and our groups were small in size, it is difficult to establish how the genotype at this SNP affects the development of diverticulitis and is at higher risk for surgical treatment. At this stage, we can form the hypothesis that patients with diverticular disease which carry the G allele have a higher risk of developing inflammatory complications, and could require subsequent surgical treatment; or, that patients carrying the A allele exhibit a lower inflammatory response and do not require surgical intervention.

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Disclosure: Nothing to disclose

P0807

PROGRESSION RATE OF DIVERTICULOSIS AND DIVERTICULAR DISEASE: PRELIMINARY RESULTS FROM AN ITALIAN NATIONWIDE REGISTRY (REMAD) AT A MEDIAN 3-YEAR FOLLOW-UP

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Introduction: Natural history of diverticulosis and diverticular disease (DD) is poorly known, and available data derived mostly from retrospective studies. Particularly, doubts subsist on the progression to DD and its complications.

Aims & Methods: Aim of this study was to assess the incidence of symptomatic uncomplicated diverticular disease (SUDD), acute diverticulitis (AD), and recurrence of diverticulitis in a cohort of patients with colonic diverticula. GrIMAD (Italian Study Group on DD) promoted the creation of REMAD (Diverticular Disease Registry), an ongoing 5-yr prospective, observational, cohort study, involving 47 centers, with follow-up assessment scheduled every six months (Trials.gov:NCT03325829).

Patients were categorized according to the following criteria:

- diverticulosis: presence of diverticula in the absence of abdominal symptoms;
- SUDD: recurrent abdominal symptoms as abdominal pain and/or changes in bowel habit, attributed to diverticula in the absence of overt inflammation;
- previous diverticulitis (PD): patients who have experienced at least one episode of diverticulitis in the past.

The incidence of new cases of SUDD and diverticulitis, as well as diverticulitis recurrence, were evaluated at a median 3.04-yr follow-up time.

The Kaplan-Meier analysis and the Cox hazard model were used in order to identify patient- and clinical-related factors associated with the progression of diverticular disease (age: ≥ 60 vs < 60 yrs; gender; BMI: ≥ 30 vs < 30 kg/m²; first-degree family history of DD or colonic cancer; active smoking; alcohol and coffee use; physical activity: active vs inactive).

Results: One-thousand and 94 (89.9%) out of the 1,217 patients enrolled in the study entered the follow-up (baseline diagnosis: diverticulosis 57.7%, SUDD 25.6%, and PD 16.7%; 46.3% females; 66.0 $\pm$ 9.7 yrs; BMI 26.1 $\pm$ 4.0 kg/m²). The cumulative incidence ($\pm$ SE) of new cases of SUDD at 3 yrs was 9.8 $\pm$ 1.3% (5.3 $\pm$ 0.9% and 7.2 $\pm$ 1.1% at 1 and 2 yrs, respectively). The 3-yr cumulative incidence of new cases of diverticulitis in patients with a baseline diagnosis of diverticulosis or SUDD was 1.6 $\pm$ 0.5% (0.9 $\pm$ 0.3% and 1.3 $\pm$ 0.4% at 1 and 2 yrs, respectively).

First degree family history of DD was a significant risk factor for developing diverticulitis (HR 2.97, 95% CI 1.19-7.38, P=0.019). After 3 yrs of follow-up, 23.1 $\pm$ 3.5% of PD patients developed a recurrence of acute diverticulitis (AD: 9.9 $\pm$ 2.3% and 16.5 $\pm$ 2.9% at 1 and 2 yrs, respectively).

Female gender was significantly higher in patients who developed AD recurrence (HR 1.91, 95% CI 1.01-3.60; P=0.043).

Conclusion: These preliminary results from a registry study suggest a low progression rate from diverticulosis to SUDD, with the latter occurring only in one patient out of ten. Furthermore, the overall incidence of diverticulitis was very low (1.6% after 3 yrs), but diverticulitis recurrence represented an important clinical challenge (23% after 3 yrs), that should be better addressed in clinical practice.

Disclosure: Nothing to disclose

P0808

ASSOCIATION BETWEEN DIETARY, LIFESTYLE FACTORS, BOWEL HABITS AND THE RISK OF COLONIC DIVERTICULITIS

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Introduction: Colonic diverticulitis is one of the most common complications of symptomatic diverticular disease frequently seen in the outpatient and inpatient settings [1]. The prevalence of diverticulitis has increased dramatically over the past several decades. It is estimated that 1-4% of patients with colonic diverticulosis will develop diverticulitis [2]. Despite the ever-growing burden on National Health Care systems worldwide [3], its pathophysiology remains poorly understood. During the last decade, a number of different risk factors have been associated with symptomatic diverticular disease including obesity, physical inactivity, and a low-fiber diet [4-8]. However, risk factors for diverticula development are likely different from those for inflammation and high-powered comprehensive analysis of different dietary and environmental factors linked with diverticulitis is lacking [9]. Therefore, the aim of our study was to investigate the association between potential risk factors and the prevalence of diverticulitis using inclusive data from a large multicenter colonoscopy-based study.

Aims & Methods: The research was conducted at three tertiary referral centers in Germany and Lithuania. Our study included consecutive adult patients referred for routine colonoscopy who completed a detailed questionnaire on diet, bowel habits, and various lifestyle aspects. We considered multiple risk factors for diverticulitis including diet (portion size, amount of meals per day, amount of fluids, amount of fish and red meat per week, etc.), frequency of bowel movements, various symptoms of constipation, tobacco use, alcohol use, nonsteroidal anti-inflammatory drug (NSAID) use, education, obesity, age, and gender. The link between risk factors and colonic diverticulitis was assessed using logistic regression and standard hypothesis testing methods where pertinent.

Results: The study included 858 patients with colonic diverticulosis, 424 (49.4%) males with a mean age of 64.92 years, and 434 (50.6%) females with a mean age of 67.83 years. Colonic diverticulitis was diagnosed in 198 (23.1%) of patients. Multivariate analysis revealed that older participants had reduced odds (OR 0.921, 95% CI 0.89-0.95, p< 0.05) of diverticulitis compared to younger subjects. In accordance with previous findings, feeling of incomplete bowel emptying after defecation was also associated with increased odds (OR 2.769, 95% CI 1.35-5.7, p< 0.006) for diverticulitis. Moreover, participants with higher educational status had increased odds (OR 2.453, 95% CI 1.31-4.59, p=0.005) for diverticulitis compared to the less educated group. Univariate analysis also showed a significant association between colonic diverticulitis and abdominal cramps (p< .0001), painful bowel movements (p=.006) and everyday tobacco use (p=.004); however, these associations were not significant in the multivariate logistic regression. Likewise, we did not find a significant association between colonic diverticulitis and gender, NSAID use, alcohol use, various symptoms of constipation, and different dietary aspects.

Conclusion: Our analysis using large well defined patient cohort establish younger age, higher education and feeling of incomplete bowel emptying as the main risk factors associated with colonic diverticulitis.

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Disclosure: Nothing to disclose

P0809

PREVALENCE OF SEGMENTAL COLITIS ASSOCIATED WITH COLONIC DIVERTICULOSIS (SCAD): AN OBSERVATIONAL STUDY IN A SINGLE TERTIARY CENTRE

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Introduction: A small proportion of patients with colonic diverticulosis may develop segmental colitis associated with diverticulosis (SCAD). SCAD is a defined pathological condition with specific macroscopic (erythema, friability and ulcerations) and microscopic features characterized by chronic, mucosal inflammation involving the inter-diverticular mucosa (usually sigmoid colon) sparing the proximal colon and rectum. Rectal and descending colon biopsies are mandatory to distinguish SCAD from inflammatory bowel disease (IBD) or others conditions. Currently, data regarding SCAD prevalence are scarce.

Aims & Methods: The aim of the present study was to assess the prevalence of SCAD in consecutive patients with colonic diverticulosis underwent colonoscopy, in a single tertiary centre.

From September 1, 2019 to February 28, 2020, consecutive patients whose colonoscopy showed endoscopic signs of inter-diverticular mucosa inflammation (erythema, friability and ulcerations) were prospectively enrolled. Biopsies were taken on the borders of the diverticula, in the apparently normal adjacent mucosa as well as, in both the colon proximal to the diverticular area and rectum (at least 8 samples). Histological evaluation was performed by an experienced pathologist. SCAD was defined by the presence of chronic inflammatory damage of inter-diverticular mucosa (increased lympho-plasmacellular infiltrate, basal plasmocytosis and basal lymphoid aggregates, neutrophilic cryptitis, crypt abscesses and crypt distortion). Inflammatory changes sparing the proximal colon and rectum mucosa allowed differential diagnosis with IBD lesions.

Clinical features, including demographic, reasons for colonoscopies in diverticulosis and *suspected-SCAD* patients were collected (ClinicalTrials.gov ID: NCT04279821).

Results: Three-hundred and 67 (26.6%) out of the total 1383 patients underwent colonoscopy presented diverticulosis [total patients: female n=711(51.4%), mean age 62.7±14.8 yrs].

Among diverticulosis patients, 4.3% (n=16) presented macroscopic signs of inter-diverticular mucosa inflammation of sigmoid colon (100% erythema, 6.7% erosions plus fibrin) and were identified as *suspected-SCAD*. *Suspected-SCAD* patients were younger (62.9± 12.9 yrs vs 69.2±10.6 yrs P=0.02), but no gender differences were found (female 56.3 vs 49.3% P=0.61), comparing to all patients with diverticulosis. No significant differences regarding reasons for colonoscopy between *suspected-SCAD* and diverticulosis patients were found [CRC screening 56.3 vs 64.8% (P=0.59); anemia 6.2 vs 9.3% (P=1,00); positive faecal occult blood 18.8 vs 12.8% (P=0.45); rectal bleeding 12.5 vs 7.1% (P=0.32); haematochezia 6.2 vs 1.1% (P=0.19); abdominal pain 0 vs 2.7%(P=1,00); changes in bowel movements 0 vs 2.2%(P=1,00)].

No patient with *suspected-SCAD* was confirmed at histology examination as SCAD. One patient received a diagnosis of Crohn's disease (sigmoid and rectum), and another one had histological features compatible with spirochetosis infection (sigmoid and rectum). The remaining patients showed non-specific mucosal inflammation, involving both sigmoid and rectum.

Conclusion: These data showed that less than 5% of diverticulosis patients were identified as *suspected-SCAD*, but none was confirmed at histology examination. A correct biopsy sampling is mandatory to confirm the diagnosis of this rare condition, thus only endoscopic SCAD diagnosis is questionable.

Disclosure: Nothing to disclose

P0810

OXIDATIVE STRESS DRIVES MYOGENIC ALTERATIONS IN DIVERTICULAR DISEASE

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Introduction: Colonic dysmotility has an important role in the pathogenesis of diverticular disease(DD). However, specific myogenic cellular mechanisms remain largely unknown.

Aims & Methods: This study aimed to investigate the molecular and morpho-functional alterations in sigmoid colon of patients affected by complicated diverticular disease(CDD). Surgical specimen were obtained from CDD, both from the stenotic (sCDD) and non-stenotic tracts (nsCDD)(n=8) and from normal tissue (CTR)(n=7), collected in macroscopically spared tissue proximal to sigmoid cancer. Longitudinal and circular muscle tissues and cells were analysed separately for: 1) western blot analysis of oxidative stress-related and inflammatory proteins: DNP as oxidized proteins; Superoxide dismutase (SOD), Catalase (CAT) and tioredoxin (TRX) as antioxidant enzymes; HMGB1, RAGE and NLRP3 as inflammatory molecules; 2) qPCR analysis of mRNA encoding for smooth muscle cells (SMC) phenotypic switch markers: Collagen I (Coll I), α-SMA, Myosin heavy chain (MHC); 3) image micrometry analysis for muscle functional activity (maximal acetylcholine-induced contraction and VIP-induced relaxation) in SMC. Data (mean±SE) are expressed as variations from CTR, except that of qPCR analysis expressed as Relative Quantification.

Results: In sCDD, an increase in DNP concentrations was observed in circular (2.95 ± 1.56) and longitudinal muscle (4.31 ± 1.77), compared to specific CTR, paralleled to a loss in antioxidant capacity that occurred both in circular (CAT: 0.51 ± 0.12 ; SOD: 0.8 ± 0.25 ; TRX: 0.77 ± 0.2) and longitudinal (CAT: 0.77 ± 0.31 ; SOD: 1 ± 0.29 ; TRX: 0.51 ± 0.1) layers. Similar oxidative stress imbalance was observed in nsCDD tissues with homogenous increase in DNP concentrations paralleled to a loss in antioxidant enzymes in both layers. No alterations in inflammatory proteins content were observed in longitudinal muscle, both in sCDD and nsCDD, while in circular muscle, the only inflammatory alteration consisted in a decrease in HMGB1 (0.08 ± 0.04 vs CTR) in sCDD. qPCR analysis carried out on SMC isolated from sCDD highlighted the presence of phenotypic switch markers in both muscle layers, with a higher involvement of longitudinal muscle. In longitudinal SMC, the expression of the contractile marker MHC was reduced to 0.28 ± 0.04 while that of the myofibroblast marker α -SMA and Coll I were increased (3.78 ± 1.87 and 5.72 ± 1.54 respectively). In circular SMC, the decrease in MHC expression was 0.58 ± 0.08 , while the increase in α -SMA and Coll I were 1.60 ± 0.58 and 1.63 ± 0.61 respectively. In nsCDD, qPCR showed in longitudinal SMC alterations similar to that observed in sCDD, while in circular SMC only an increase in Coll I expression was found, without alterations in MHC and α -SMA. Differences in phenotypic switch markers expression between the two muscle layers were significant ($p < 0.05$), both in sCDD and nsCDD. Finally, functional alterations were observed only on longitudinal SMC both in sCDD and nsCDD. Contraction was inhibited by $38.4\% \pm 7.1$ in sCDD and $31.6\% \pm 6.2$ in nsCDD while relaxation by $40.4\% \pm 14.2$ and $26.5\% \pm 3.2$ in sCDD and nsCDD, respectively.

Conclusion: In sCDD and nsCDD, an oxidative stress imbalance with loss of antioxidant capacity occurs in both circular and longitudinal muscle layers associated to a switch of SMC from the contractile phenotype, that mainly involves the longitudinal muscle. These myogenic perturbations might impair colonic compliance and potentially increase intraluminal pressure, key factors in DD pathogenesis. The evidence of an oxidative stress contribution in myogenic impairment could open new possible therapeutic strategies.

Disclosure: Nothing to disclose

P0811

10-YEAR EVALUATION OF A NATIONAL COHORT OF 360 PATIENTS TREATED BY SACRAL NERVE MODULATION FOR FECAL INCONTINENCE: RESULTS OF A FRENCH MULTICENTRE STUDY

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Introduction: Sacral nerve modulation (SNM) is the second line therapy for patients with fecal incontinence (FI). However, few studies have evaluated the long-term success of SNM.

Aims & Methods: The objective of the present study was to assess the effectiveness of sacral nerve modulation (SNM) in a large cohort of patients implanted for at least 10 years, quantify the rate of adverse events rate and to identify the predictive factors of long-term success. The prospectively collected data of patients implanted for FI in 7 French centres between January 1998 and December 2008 were retrospectively analysed. Patients had FI severity scores completed before and 10 years after implantation. The main evaluation criterion was the success of the SNM defined by the continuation of treatment without additional therapeutic. The secondary evaluation criteria were the rate of revisions and explantations. Pre-operative predictors of success at 10 years were sought.

Results: Of the 360 patients (27 males, mean age: = 59 ± 12 years) implanted for FI, 162 (45%) were still treated with SNM 10 years after implantation, 115 (31.9%) failed and 83 (23.1%) were lost to follow-up. In the favourable outcome group, FI severity scores were significantly improved 10 years after implantation compared to pre-implantation ($P < 1.10^{-4}$). During the 10-years follow-up, 233 patients (64.7%) had a surgical revision and 94 (26.1%) were explanted. Previous surgeries for FI were the only negative predictive factor identified.

Conclusion: A least 10 years after implantation long-term efficacy of SNM could be maintained in 45% of patients with FI selected for SNM.

Disclosure: Drs. Damon, Meurette, Faucheron, Siproudhis, and Leroi are members of the scientific committee of the Medtronic registry on faecal incontinence. Paul Lehur has a consultancy agreement with Medtronic SA and B.Braun. C Brochard received lecture fees from IPSEN.

P0812

CLINICAL AND PSYCHOLOGICAL CORRELATES OF FUNCTIONAL ANORECTAL PAIN

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Introduction: Functional anorectal pain (FARP) is a common functional disorder separated into three different disorders: Levator Ani Syndrome, Proctalgia Fugax, and Nonspecific proctalgia. The present study aimed to search the psychological and clinical factors associated with functional anorectal pain according to the phenotype.

Aims & Methods: This retrospective observational study included 2358 patients presenting to a tertiary center with 411 patients having FARP. All the patients completed the Rome III questionnaire, four Likert scales for symptoms severity for constipation, diarrhea, bloating, and abdominal pain, Bristol stool form, Depression, and Anxiety. Statistical analyses with logistic regression and multinomial logistic regression were used to model the relationship between anorectal pain phenotypes, with the recorded parameters.

Results: 159 patients had Levator Ani Syndrome, 142 Proctalgia Fugax, and 110 nonspecific anorectal pain. FARP patients were characterized by higher depression ($P=0.009$), higher prevalence of globus ($P=0.024$), postprandial distress syndrome ($P=0.034$), aerophagia ($P=0.015$), IBS ($P<.001$), and higher severity for constipation ($P=0.003$), diarrhea ($P=0.003$) and abdominal pain ($P<.001$). Levator Ani Syndrome patients had higher postprandial distress syndrome ($P=0.011$) and reported higher severity for diarrhea ($P=0.040$), and abdominal pain ($P=0.001$). Nonspecific anorectal pain patients reported higher severity for diarrhea ($P=0.015$) and abdominal pain ($P<.001$). Proctalgia Fugax patients had higher aerophagia ($P=0.033$) and IBS ($P=0.016$), higher severity for constipation ($P=0.001$), and abdominal pain ($P=0.048$).

Conclusion: This study showed the importance of depression and the association of FARP with upper functional disorders or bowel disorders according to the phenotype.

Disclosure: Nothing to disclose

P0813

ADDED VALUE OF ENDOSONOGRAPHY IN THE STUDY OF ANAL INCONTINENCE: A PICTORIAL ESSAY

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Introduction: Anal incontinence is usually assessed through a combination of digital examination and physiological tests. Endoanal ultrasound (EAUS) constitutes an excellent method for sphincter evaluation; perineal ultrasound can provide additional insight on both the anatomy and physiology of the anal canal. This study aims to determine the role of EAUS and perineal ultrasound in the evaluation of anal incontinence.

Aims & Methods: Consecutive patients with incontinence of solid stool referred to our unit for endosonographic study were enrolled. Aetiology was defined as idiopathic, obstetric or traumatic. Wexner score was calculated and Bristol stool scale was used. EAUS was performed using a rigid probe (Hitachi Medical Systems). Their medical records, EAUS and perineal ultrasound reports and additional imaging records were reviewed.

Results: A total of 28 subjects were included (female - 75%; mean age - 61.9 years; mean Wexner Score 7.2 points). Digital examination was performed in all patients and anal sphincter tone at rest was described as reduced in 7 patients (25%). EAUS and perineal ultrasound were performed in all patients; complementary evaluation with 3D-reconstructions, elastography and endovaginal ultrasound were performed when deemed necessary by the operator.

EAUS showed anal sphincter defects in 9 out of 28 patients (32.1%). In the 19 remaining patients, abnormal findings were present in 36.8%, being rectocele the most common finding (4 patients). Overall, ultrasonographic study of the anal canal showed abnormal findings in 16 out of 28 patients (57.1%). No complications occurred.

Conclusion: In this study, endosonographic study of the anal canal has revealed significant abnormalities in patients with anal incontinence. EAUS and perineal ultrasound should be considered in the routine investigation of these patients.

Disclosure: Nothing to disclose

P0814 WITHDRAWN

P0815

RANDOMIZED TRIAL COMPARING POLIDOCANOL FOAM SCLEROTHERAPY WITH RUBBER BAND LIGATION IN THE TREATMENT OF FIRST, SECOND AND THIRD-GRADE HEMORRHOIDAL DISEASE

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Introduction: Hemorrhoidal disease (HD) is a benign condition seen frequently in clinical settings. Rubber band ligation (RBL) and sclerotherapy have proven to be the office-based procedures of choice in HD, with various studies reporting RBL as being more effective but also more painful and bleeding prone than sclerotherapy with liquid polidocanol. To date, there are no studies comparing RBL with sclerotherapy with polidocanol foam, a new type of sclerosant agent that has already proved to be more effective and safer than liquid polidocanol in grade I HD.

The present study was designed to establish the clinical effectiveness and safety of polidocanol foam sclerotherapy compared with RBL.

Aims & Methods: This randomized controlled trial included patients with symptomatic HD grades I to III. A sample size of 120 participants was determined. Patients, stratified by HD grade, were randomly assigned (1:1 ratio) to either RBL or polidocanol foamsclerotherapy.

During the 3-months intervention period the patients were submitted to one of the procedures.

Efficacy (therapeutic success combining Sodergrenscore and bleeding grade, number of treatment sessions needed to achieve therapeutic success and HD grade evolution) and safety (complications) outcomes were evaluated.

Results: Sixty patients in each therapeutic arm were included. Efficacy outcomes revealed that sclerotherapy group had more participants having complete success (53 versus 40, $p=.0087$) and needed less office-based sessions (1.32 versus 1.62, $p=.0178$). Adverse events were more common in the RBL group (30% versus 10%, $p=.011$). No severe complications were observed in either group.

Conclusion: Both procedures are effective in the treatment of hemor-

rhoidal disease grades I to III, however participants undergoing polido-canol foam sclerotherapy needed fewer interventions, had less complications, and were more likely to become completely asymptomatic than those submitted to ligation. Follow-up (ongoing) is required to assess if this new therapy is effective in the long term.

Disclosure: Nothing to disclose

P0816

EVALUATING THE ACCURACY OF HEMORRHOIDAL DISEASE REFERRAL

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Introduction: A large proportion of patients with anorectal complaints are referred to coloproctology consultation with the label of hemorrhoids.

Aims & Methods: The purpose of this study was to review presenting symptoms and frequency of accurate diagnosis, comparing the different specialties that refer patients to coloproctology consultation. Determinants of misdiagnosis were analyzed to guide educational endeavors.

Methods: Retrospective study, which included patients referred for coloproctology consultation between January 2017 and September 2019 with a diagnosis of hemorrhoids. Symptoms of presentation and anal examination at the time of referral were collected and evaluated. Then, accuracy of the diagnosis of hemorrhoids was assessed.

Results: 109 patients with the referral diagnosis of hemorrhoids were included.

The most common presenting symptoms were bleeding (55%; n = 80), pain (29%; n = 43) and protrusion (10%; n = 14).

Anal examination (ie, external inspection and/or digital internal examination) before referral for coloproctology consultation was documented in only 47%.

The hemorrhoid diagnostic accuracy was 66% (n = 72).

Among patients with incorrect hemorrhoid diagnoses (34%), actual diagnosis was anal fissure (57%), skin tag (24%), rectal and anal polypoid lesions (11%) and hypertrophied papilla (8%). Among patients referred from general practitioners (N = 62), 43.5% (N = 27) had a wrong diagnosis of hemorrhoids, while patients referred from other specialties (N = 47), only 23.4% (N = 11) had a wrong diagnosis.

Compared to other specialties, patients referred from general practitioners are at a higher risk of a wrong diagnosis (OR 1.86 (95% CI, 1.03-3.36); p = 0.02).

Conclusion: A variety of anorectal complaints are diagnosed as hemorrhoids by providers who have initial contact with the patients. General practitioners were the group that most referenced patients with a wrong diagnosis of hemorrhoids.

Educational programs directed toward improving physician knowledge are needed once they can potentially improve diagnostic accuracy and earlier initiation of appropriate care.

Disclosure: Nothing to disclose

P0817

MEAN PLATELET VOLUME, NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO AS AN INFLAMMATION MARKERS REFLECTING THE SEVERITY OF PERIANAL ABSCESES

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Introduction: Perianal abscesses are common anorectal problems. The infection originates most often from an obstructed anal crypt gland, with the resultant pus collection. The most typical symptoms of that disease are severe pain, fever and palpable mass in rectal examination. There are some imaging examinations like pelvic CT scan, MRI or trans-rectal ultrasound, which are conducted to specify the location and size of perianal abscess.

However, a quick and easily available parameter relating to the severity of abscess could become helpful for clinicians treating patients with perianal abscesses.

Aims & Methods: To determine if mean platelet volume (MPV), neutrophil lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), easy available parameters from complete blood count (CBC) test, can be useful inflammatory biomarkers reflecting the severity of perianal abscesses.

Materials and methods: Retrospective study was conducted on 130 patients. The data was collected from patients who were hospitalized in the Department of General and Colorectal Surgery at Medical University of Łódź. Patient's gender, age, medical diagnosis as well as their chronic diseases and smoking were recorded.

Parameters before surgery such as MPV, NLR, PLR and the amount of pus collected from abscess incision were also analyzed. Patients were divided into two subgroups based on amount of drained pus during surgery: 1 group with purulent drainage ≤ 30 mL and 2 group with purulent drainage >30 mL.

Results: One hundred and thirty were enrolled in this study, including 67 patients in first group and 63 patients in second group. The MPV level was significantly higher in the group with greater amount of drainage than in the second group (10,67±0,95 vs. 10,12±0,86, p=0,004). NLR and PLR were also elevated in first group (6,22±2,8 vs. 4,47±1,9, p< 0,001; 187,35±65,27 vs. 167,08±70,81 p=0,036 respectively).

Conclusion: The MPV, NLR and PLR were higher in patients with greater amount of purulent drainage. Mentioned parameters reflected the severity of perianal abscess. The MPV, NLR and PLR may thus be indicators of perianal abscess severity.

Disclosure: Nothing to disclose

P0818

DISSYNERGIC DEFECATION: AN UNDERVALUED DIAGNOSIS IN QUIESCENT ULCERATIVE COLITIS

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Introduction: The overlap of Inflammatory Bowel Disease (IBD) symptoms and Defecation Disorder (DD) may be highly prevalent, though its diagnosis in patients with quiescent IBD remains a challenge due to clinical under-

valuation or the association of these symptoms with IBD. Identification and proper management of DD in IBD can significantly improve patients' quality of life and decrease health care resources consumption.

Aims & Methods: We aimed to determine the prevalence of DD in quiescent Ulcerative Colitis (UC) and characterize these patients to attain an earlier recognition in clinical practice. Thus, a unicentric, prospective, case-control study was performed in the Gastroenterology department of Braga Hospital in 2019. Patients with quiescent UC with persistent anorectal symptoms were selected. The control group was selected from a prospectively collected database at the Proctology consultation. Besides the gold standard physiological tests (anorectal manometry and/or defecation imaging), digital rectal examination and balloon expulsion test were also performed.

Results: From the 488 patients with quiescent UC, 7.8% (n=38) revealed ongoing anorectal symptoms, mainly constipation (94.7%; n=36). Most patients were female (81.6%), with a mean age of 51.9 years old. Regarding UC, the disease extension was limited to the rectum in 60.5%, with an average disease duration of 14 years, in remission with 5-aminosalicylic acid (92.1%). Following clinical and physiological evaluation, DD was diagnosed in 48.4% of the patients, mainly Dyssynergic Defecation (86.7%), which was significantly higher than in the control group (p=0.033). Disease duration revealed to be an independent risk factor for Dyssynergic Defecation in UC (OR: 1.08; p=0.041).

Conclusion: DD are highly prevalent in quiescent UC with ongoing anorectal symptoms, mostly present in patients with long-standing UC. Dyssynergic Defecation is the most frequent etiology and its early recognition will allow a proper treatment with biofeedback therapy

Disclosure: Nothing to disclose

P0819

SYSTEMATIC CHARACTERIZATION OF DEFECOGRAPHIC ABNORMALITIES IN A CONSECUTIVE SERIES OF 827 PATIENTS WITH CHRONIC CONSTIPATION

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Introduction: Barium defecography can assess structural and functional abnormalities in patients with chronic constipation.

Aims & Methods: We aimed to determine the prevalence of individual and overlapping defecographic findings by systematic evaluation of images with results stratified by sex. Consecutive examinations of 827 consecutive patients presenting over a 30-month period with well-defined symptom severity (≥ 12 points on the Cleveland Clinic Constipation score) were analysed. Six individual functional or anatomical (intussusception, rectocele, enterocele, megarectum, excessive dynamic perineal descent) defecographic observations were defined *a priori* thus permitting 64 possible combinations of findings (i.e. 63 abnormal types + 1 normal).

Results: Patients with constipation (mean symptom score 19) were predominantly female (88%) with median age 49 (17-98) years. All 6 individual radiological findings were identified with a total of 43 combinations found

in the cohort; the 14 most prevalent of these accounted for >85% of patients. Only 136 (16.4%) patients had a normal defecography (34.3% males vs. 13.9% females; $P < 0.0001$). Overall, 612 (74.0%) patients had structural (n=508 [61.4%]) or functional (n=104 [12.6%]) abnormalities in isolation, with 79 (9.6%) others exhibiting combinations of both. Functional abnormalities in isolation were more common in males compared to females (22.5% vs. 11.2%, $P=0.025$) as opposed to structural abnormalities (57.8% vs. 85.7%, $P < 0.0001$). Expulsion time was longer in females compared to males (110 [60-120] vs. 90 [60-120] sec; $P=0.049$).

Conclusion: These results provide a contemporary atlas of defecographic findings in constipation. Several individual structural and functional features have been systematically classified, with overlap greater than previously acknowledged and implications for tailoring surgical planning.

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Disclosure: Nothing to disclose

P0820 WITHDRAWN

P0821

USEFULNESS OF C.ELEGANS FOR GASTROINTESTINAL CANCER SCREENING TEST BASED ON SMELL OF URINE SAMPLE

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Introduction: Early detection of cancer is important, and a low-cost and highly accurate method is required. The problem with classic biochemical markers is their low sensitivity to detect early-stage cancers. The olfactory behavior of the *Caenorhabditis elegans* (C.elegans) to human urine can be utilized to discriminate patients with cancer from healthy people. A novel cancer screening test based on the olfactory response of C. elegans named Nematode-NOSE (N-NOSE).

A previous study reported that N-NOSE is highly capable of detecting early-stage cancers. In this study, we compared the detection ability of N-NOSE to that of tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9).

Aims & Methods: From May 2017 to November 2019, N-NOSE was performed on urine samples from 48 cancer patients and 15 healthy volunteers who agreed to participate in this study. The patients were diagnosed with one the following cancer types: stomach, colorectal, liver, biliary tract, pancreatic, or esophageal cancer. We examined the detection sensitivity for each cancer type and stage.

Additionally, we compared the accuracy of N-NOSE to classic biochemical markers (CEA and CA19-9) for the screening of gastric, colorectal, biliary, and pancreatic cancers.

Results: N-NOSE showed a high sensitivity of 75.0% (36/48) among all cancer types. The usefulness of N-NOSE was statistically significant in detecting the presence or absence of cancer (t-test, $p = 0.0038$). The sensitiv-

ity for each cancer type was high, as follows: 72.7% (8/11), 88.9% (16/18), 66.7% (4/6), 100% (3/3), 50% (3/6), and 50.0% (2/4) for gastric, colorectal, liver, biliary tract, pancreatic, and esophageal cancer, respectively. The sensitivity for each stage was as follows: 66.7% (2/3), 81.8% (9/11), 42.9% (3/7), and 81.5% (22/27) for Stage I, Stage II, Stage III, and Stage IV, respectively. The sensitivity of N-NOSE to detect early stages of cancer was higher than that of tumor makers.

Conclusion: N-NOSE showed high sensitivity in detecting early to late stage cancers, suggesting that it could be used as a noninvasive and simple cancer risk test.

Disclosure: Nothing to disclose

P0822

MANAGEMENT AND LIMITATIONS OF SELF-TREATED CONSTIPATION - THE VIEW OF GERMAN HEALTH CARE PROFESSIONALS

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Introduction: Chronic constipation is a common problem affecting up to 15% of the German population each year [1]. Symptoms are often managed successfully with prescription-free drugs. However, little is known on healthcare providers (HCPs) view on management and limitations of an ongoing self-medication approach taken by patients for their constipation symptoms.

Aims & Methods: An online survey was performed (FEB-MAR 2020) in Germany to better understand the attitude of different HCPs regarding opportunities and limitations of constipation management within self-care. 300 HCPs were interviewed on the Doc-Check Research platform using a randomized sample of an expert panel (n=100 office-based General Practitioners (GP), n=100 Pharmacists (PH) and n=100 Pharmacy Technicians (PTA)).

Results: When asked *if treatment of acute constipation is suitable for self-medication (in the absence of alarm symptoms such as blood in stool, severe abdominal pain, sudden weight loss)*, the majority of HCPs “agreed” or “fully agreed” (GP: 73%, PH: 84%, PTA: 73%). When asked *if chronic constipation can be self-treated for a longer time period and under patients responsibility (after initial physician consultation and doctor’s referral if there is a noticeable change in symptoms)*, again, the majority of HCPs “agreed” or “fully agreed” (GP: 73%, PH: 83%, PTA: 70%; categories: fully agree/agree/neither nor/do not agree/do not agree at all). Interestingly, several respondents did “not agree”/ “not agree at all” on the statements above (suitability of self-medication: acute constipation GP 14%, PH: 10%, PTA: 23%; chronic constipation GP 11%, PH: 5%, PTA: 15%).

When asked *for the right timeframe for doctor’s referral*, most respondents considered 1 month or longer as appropriate (GP: 80%, PH: 73%, PTA: 65%). Notably, 24% of GPs indicated that no medical clarification would be necessary if no change in symptoms occurred (for more information see Table 1A). By contrast, statements for re-consultation in case of chronic constipation showed a diverse pattern. Most GPs considered either 3 months (33%) or no additional consultation (31%) as the right behavior. PH respond similarly to GPs whereas only 8% of PTAs responded with “no additional medical clarification” would be necessary in such cases (Table 1B).

1A	A person with constipation: under control by means of self-medication, without any other health problems or warning signals			1B	A person with chronic constipation: symptoms under control with self- medication and initial medical consultation was performed		
	HCPs				HCPs		
	GP	PH	PTA		GP	PH	PTA
after 1 week	11 %	10 %	14 %	after 3 months	33 %	22 %	40 %
after 2 weeks	9 %	17 %	21 %	after 6 months	16 %	33 %	27 %
after 1 month	24 %	29 %	33 %	after 1 year	12 %	17 %	19 %
after 3 months	21 %	18 %	18 %	after 2 years	8 %	5 %	6 %
after 6 months	11 %	6 %	6 %				
No medical clarification necessary as long as no change in symptoms	24 %	20 %	8 %	No medical clarification necessary as long as no change in symptoms	31 %	23 %	8 %

[Table 1A: Time after which medical clarification is considered necessary/
1B: Time after which a renewed medical clarification is considered necessary]

Conclusion: Most GPs, Pharmacists and PTAs confirm that constipation is suitable for self-treatment, even for a longer time-period, in the absence of “red flags” respectively after initial doctor consultation (chronic constipation). Within the HCP categories we recognized a strong partition between responders being progressive or very defensive in terms of suitability of self-medication treatment for constipation and the necessity for an additional diagnosis.

We therefore believe that expert guidance would be helpful for both, patients and HCPs, to give clear recommendation regarding management and limitations in self-treating constipation.

References: [1] Enck P et al. Prevalence of constipation in the German population - a representative survey (GECCO). UEG J. 2016; 4: 429-437

Disclosure: Landes S., Biber-Feiter D. and Plomer M. are employees of Sanofi-Aventis; Frieling T. has been consultant/speaker for Bayer AG, Falk, Janssen-Cilag, Sanofi-Aventis, Shire, Steigerwald, Schwabe Pharma; Martin E. has been consultant/speaker for Astra Zeneca, Berlin Chemie, Infectopharm and Sanofi-Aventis, Pohl D. has been consultant/speaker or received research support from Medtronic, Permamed, and Sanofi-Aventis; Ude C. has been consultant/speaker for Bionorica, Infectopharm Arzneimittel und Consilium, Sanofi-Aventis, Schwabe.

P0823

REAL WORLD EXPERIENCE OF FAECAL IMMUNOCHEMICAL TESTING (FIT) IN UK PRIMARY CARE TO SUPPORT THE REFERRAL AND DIAGNOSIS OF COLORECTAL CANCER (CRC)

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Introduction: Symptoms of CRC, particularly at an early stage of disease, can be difficult to recognise. In the UK, NICE recommends referral for investigation based on high risk (NG12)¹ criteria and lower risk symptoms, which in 2018 were revised to include the use of FIT testing for low risk patients defined by DG30².

Aims & Methods: This observational cohort study aims to assess the use, impact and diagnostic accuracy of FIT testing in our local community, following the implementation of NICE DG30 guidance for patients aged over

50yr old. Patients submitting a FIT test were identified from a single clinical biochemistry data set (serving the entire local population of 1.2million) and cross referenced with endoscopy, radiology and e.health records. Relevant demographic, clinical and laboratory data were extracted and merged into a single data set which was cross-referenced with Cancer Registration data. FIT samples were collected and analysed with OC Sensor, using a cut off 10µgHb/gm in line with NICE recommendations.

Results: From April-Dec 2019, 1083 FIT tests were analysed, of which 823 (76%) were < 10µgHb/gm. Over the same time period 3,612 patients with suspected CRC (median age 70, range 24-97yrs old) were referred, of whom 256 had a FIT test done as part of the referral. From this group, 143/256 patients had a positive test, of whom 10/143 (7%) were subsequently found to have CRC. Other findings in patients with a FIT >10µgHb/gm included significant bowel pathology (advanced adenoma/IBD, n=27) or (normal n=25 or other incidental findings n=74). 7 patients were not assessed by colonoscopy or CTC due to frailty or multiple co-morbidity or declined further investigation. Patients with a FIT > 100µgHb/gm were 7x more likely to have CRC than those with FIT between 10-100µgHb/gm (p=0.002). Otherwise median (range) FIT values did not differ significantly between other identified pathologies or those with normal findings. Amongst patients with a FIT < 10µgHb/gm (n=823), 113 (13.7%) were nevertheless referred due to clinical concern including 1 patient with anaemia and thrombocytosis who subsequently was found to have an early caecal adenocarcinoma. Cross referencing with Cancer Registration data confirmed no missed cancer diagnoses. Overall, patients with any lower GI symptoms and a FIT>10µgHb/gm had a 7% risk of CRC, compared to 0.9% in patients with a FIT < 10µgHb/gm. Interestingly, FIT testing was often done by family physicians (GPs) in patients with high risk NG12 symptoms (40% of patients) and without regard to the age criteria for testing (13% of patients referred).

Conclusion: Our real world data confirm that FIT is a useful test in identifying those patients who need further investigation for suspected CRC. Further research into the use of FIT in the diagnosis of CRC is needed, particularly to support appropriate uptake and implementation in primary care.

References: 1)<https://www.nice.org.uk/guidance/ng12> 2)<https://www.nice.org.uk/search?q=dg30>

Disclosure: Nothing to disclose

P0824

FREQUENCY OF GAS-RELATED SYMPTOMS AND IMPACT ON QUALITY OF LIFE IN THE FRENCH GENERAL POPULATION USING THE NEWLY VALIDATED INTESTINAL GAS QUESTIONNAIRE (IGQ)

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Introduction: Available data on prevalence of gastrointestinal symptoms in the general population are limited and often coming from non-validated tools. Aim of this study was to generate first data on the frequency of gas-related symptoms and their impact on quality of life (QoL) in a representative sample of the French population using the newly validated Intestinal Gas Questionnaire (IGQ).

Aims & Methods: 1543 adults being part of the "Behaviors and food consumption in France" (CCAF) survey 2019 were recruited by phone to complete an online survey between January and July 2019. Participants were invited to provide socio-demographic characteristics and to complete the

17 item IGQ questionnaire (7 symptoms severity items and 10 impact on QoL items) and a lifestyle questionnaire. To ensure representativity of the sample, a quota-based method sampling was used considering gender, age, employment, familial status, education level, region and size of urban area. IGQ scores ranging from 0 to 100 (worse) were computed to get a total score and a score for each of the 6 dimensions (bloating, flatulence, belching, bad breath, stomach rumbling, difficult gas evacuation). Descriptive statistics and non-parametric tests (Wilcoxon signed Rank Test, Kruskal-Wallis) with a nominal Type I error of 5% were done to investigate associations between symptoms, socio-demographic characteristics and lifestyle parameters. Subjects rating at least one symptom severity item AND one impact on QoL item in the middle of the IGQ response scale (i.e. 5 on 0-10 numeric scale) were considered bothered by digestive problems.

Results: Mean (sd) total IGQ score was 11.2 (±10.8). Only 7% of individuals declared being free of any digestive symptom (IGQ total score=0). Following parameters were associated with significantly higher IGQ total scores: age (p< 0.001) with aged 18-24 having the highest scores, sedentary lifestyle (p< 0.001), employment (p< 0.001) with unemployed having the highest scores, size of urban area (p=0.042) with bigger size associated with higher scores, BMI (p=0.005) with underweight and obese having the highest scores, being on a diet (p=0.031), having allergies (p=0.006) and smoking (p=0.003). Female gender was associated with significantly higher bloating and difficult gas evacuation dimension scores (both p< 0.001). Among symptomatic individuals, 21% took an action including taking medication. Individuals mostly impacted by their symptoms represented 22% of the cohort (n=388) with a mean total IGQ score of 25.9 (±11.9).

Conclusion: Using the newly validated IGQ, we quantified for the first-time prevalence of symptoms related to intestinal gas in a representative sample of the French general population. Age, sedentary lifestyle and BMI are associated with severity of symptoms and their impact on QoL.

References: Duracinsky M et al., Gastroenterology, May 2019 Volume 156, Issue 6, Supplement 1, Page S-575

Disclosure: Boris Le Nevé, Laurent Quinquis and Bénédicte Monnerie are employees of Danone Nutricia Research; Martin Duracinsky and Olivier Chassany are consultants for Danone Nutricia Research

P0825

THE JAG SURVEY OF UK ENDOSCOPY SERVICES: RESULTS FROM THE 2019 CENSUS

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Introduction: The Joint Advisory Group on Gastrointestinal endoscopy (JAG) conduct a biennial census to understand factors related to endoscopy quality, workforce and training across services in the UK. The study reports the results of the 2019 census.

Aims & Methods: A census of all UK JAG-registered services was conducted in April 2019. Questions were devised by an expert panel covering domains of activity, workforce and waiting times. Question items were informed by results of the previous census. Results were collated and analysed using Chi Square, Fisher's exact and Kruskal Wallis tests.

Results: The response rate was 68.4%. A total of 2,133,541 endoscopic procedures were performed in 2018. In March 2019, 31,938 endoscopy lists were delivered (mean 99.2 ± 95.7 per service).

The responding services employed 5,578 endoscopists (mean 17.32 ± 10.13, 12% non-medical), 1,366 trainees (mean 4.24 ± 6.43) and 12,680 nurses and allied health professionals (AHP) (mean 39.94 ± 284.81). There was a nursing and AHP vacancy rate of 7.29%. Region ($p = 0.02$) and service type ($p < 0.001$) had a significant association with vacancy.

Out of the lists performed by trainees, 51.9% were for training only. An average of 7.46 (± 1.45) oesophago-gastroduodenoscopies and 3.86 (± 0.85) colonoscopies were booked for each training list. There was a significant regional influence on number of trainee lists ($p < 0.001$).

In the first 3 months of 2019, waiting time targets were met by 73.7% of services for urgent cancer, 68.7% for routine waits and 63.4% for surveillance waits. There was a significant difference in meeting targets between region ($p < 0.01$) and service type ($p < 0.01$). The commonest reasons for this were endoscopist, physical and nursing capacity. JAG accredited services were more likely to meet routine and surveillance wait targets than unaccredited services ($p < 0.001$). The mean standard DNA (Did Not Attend) rate for March 2019 was 3.48 (± 3.07) as shown in Table 1.

List Type	DNA rate (mean ± SD)	UK region	Service type (acute, independent or non-acute)	Accreditation status
Standard (symptomatic, surveillance, therapeutic)	3.48 ± 3.07	$p < 0.001$	$p < 0.001$	$p = 0.48$
Bowel cancer screening	1.33 ± 2.81	$p = 0.07$	$p = 0.51$	$p = 0.41$

[Table 1. DNA rates and service-related factors]

Conclusion: This census reflects the most extensive data regarding current UK endoscopy practice. There is evidence of service pressure, affecting wait times and training opportunities with significant regional and service-specific variability.

Disclosure: Nothing to disclose

P0826

A NATIONAL SURVEY OF SAFETY ACROSS UK ENDOSCOPY SERVICES

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Introduction: The 'Improving Safety and Reducing Error in Endoscopy' (ISREE) strategy has highlighted the need to improve our understanding of factors related to safety across UK endoscopy. This study assesses aspects of safety that were included in the Joint Advisory Group on Gastrointestinal endoscopy (JAG) biennial census of services.

Aims & Methods: An expert panel devised questions across 7 themes that complemented JAG safety domains. These were incorporated into the census of UK JAG-registered services in April 2019. Census results were collated and analysed. Categorical data was analysed through Chi square, Fisher's Exact, Kruskal Wallis and Friedman's tests. Free text responses were analysed thematically.

Results: The response rate was 68.4%. Across March 2019, a total of 1535 patient safety incidents (PSIs) were reported (per service mean 4.80, SD 11.87). There was a significant difference in reporting dependent on incident type ($p < 0.001$). Technical and training incidents were least likely to be reported. There was no effect of region, service type or JAG accreditation status on reporting behaviour.

Anaesthetic-supported (AS) lists were unavailable to 27% of services. This varied amongst service type ($p < 0.001$) but not region ($p = 0.13$). There was a significant difference between the current and desired number of AS lists ($p < 0.001$). There was no significant association between service type and presence of preassessment service ($p = 0.42$), sedation policy ($p = 0.685$) or presence of a sedation lead ($p = 0.08$).

The majority of acute services have a gastrointestinal bleed (GIB) service (82.2%) but provision is significantly different between regions ($p < 0.001$). Accreditation ($p < 0.01$) and AS lists ($p < 0.01$) were strongly associated with having a GIB service.

Overall, 66.1% of services reported having an effective strategy for supporting underperformance. More endoscopists require support for technical skills than non-technical skills ($p = 0.001$). Simulation provision was 49.1% across acute services, with significant regional differences ($p = 0.001$). Learning is shared following discussion of adverse events in 94.1% services. Patient feedback is used primarily to support learning, training and quality improvement.

Conclusion: This is the first survey of national endoscopy safety practice and highlights regional and service-specific variability. These results are important in guiding the ISREE strategy forwards in supporting safer UK endoscopy.

Disclosure: Nothing to disclose

P0827

COSTS OF OPIOID INDUCED CONSTIPATION FOR CANCER PATIENTS IN ENGLAND: A RETROSPECTIVE COHORT STUDY

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Introduction: Opioids are a standard treatment for pain management and palliative care in patients with cancer. However, opioids are associated with significant adverse events including opioid induced constipation (OIC) which impacts upon the quality of life of the patient and presents a significant health burden. In this study we aimed to estimate rates of OIC in cancer patients treated with opioids and to measure the extent and cost of non-stable OIC

Aims & Methods: The study was conducted in the Clinical Practice Research Datalink (CPRD); a large routine primary care database from the United Kingdom. Patients whose data could be linked to Hospital Episodes Statistics inpatient data were included. Episodes of opioid exposure of ≥ 28 days were selected from between 1st January 1998 and 31st December 2017 with date of first prescription defining index date. Opioid episodes were classified as strong, weak or a combination of weak and strong. Episodes for patients with a diagnosis of cancer recorded in the 12 months prior to index date were selected for this analysis. Constipation during the opioid episode was flagged based upon either a primary care laxative or enema prescription or inpatient hospitalisation with a diagnosis of constipation. Constipation was categorised as stable if multiple laxatives were prescribed with no augmentation, switching or dosage increase during the opioid episode. Constipation was characterised as unstable if prescriptions were intensified, an enema prescribed, or a patient hospi-

talised with a diagnosis of constipation. Episodes with a single laxative prescription were presented separately as it was not clear whether these laxatives were prescribed prophylactically. Costs in the 12 months following index date for all health contacts (inpatient, outpatient and primary care) and those relating to constipation were aggregated

Results: 33,090 opioid episodes for UK cancer patients met the study criteria. Of these episodes, 3,349 (10.1%) were classified as strong opioids, 16,900 (51.1%) as weak and 12,841 (38.8%) as a combination of weak and strong. 1,352 (40.4%) strong opioid episodes were classified as OIC of which 993 (29.7%) unstable OIC. Respective figures were 3,817 (29.7%) and 2,281 (13.5%) for weak opioids and 7,600 (62.7%) and 5,939 (46.3%) for those prescribed weak and strong. Strong opioid episodes with unstable OIC had constipation costs estimated at £700 per patient year compared to £228 for those on weak and £359 on weak and strong

Conclusion: A large proportion of UK cancer patients treated with opioids, with a significant proportion receiving strong opioids, will experience OIC. Of these many patients experience unstable OIC with subsequent increased resource use. The impact of constipation should be considered when prescribing opioids to cancer patients with an aim to stabilise their OIC to potentially reduce healthcare costs

Disclosure: This abstract is funded by Shionogi BV and Peter Conway is an employee of Shionogi BV

P0828

COMPLEX POLYP MULTIDISCIPLINARY MEETING : COMPLIANCE AND OUTCOMES

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Introduction: Complex polyp MDM (CP-MDM) was first introduced at our Trust in 2018.

It is now well-established meeting similar to other MDMs, having a standard operational policy fulfilling local governance framework and with clear complex polyp pathways in line with national guidelines.

Aims & Methods: The CP-MDM operates weekly and comprises of a CP-MDM coordinator, two Gastroenterologists, two Surgeons, a Pathologist on demand, specialist polyp nurse, bowel cancer screening nurse and booking service manager. At the CP-MDM, a clinical management consensus is reached based on the polyp surface features, co-morbidities, radiological findings and performance status of the patients.

We audited the CP-MDM for the year 2018 for the quality of referrals, the outcomes, the compliance of the CP-MDM outcomes as well as the time to intervention following the CP-MDM. Data was retrieved from the CP-MDM on electronic records, the endoscopy reports, the clinic letters, and radiology reports.

Results: 195 patients were referred to CP-MDM in 2018, including referrals from BCS and Colorectal MDM.

10 patients were removed from CP-MDM and discharged back to the referring physician (5 unfit for endoscopic intervention and another 5 declined treatment).

102 of 185 (55%) patients were referred for therapeutic endoscopy which was carried out in a single visit. 65 patients underwent piecemeal resections, 25 en-bloc dissections, 10 cold snare piecemeal resections, and 2 patients had Trans-Anal Submucosal Endoscopic Resection.

66 patients (35%) required repeat diagnostic endoscopy for better assessment of the surface polyp features.

17 patients were referred for radiologic investigations (11) and outpatient clinic (6).

24 patients were discussed twice and 6 cases were discussed thrice.

17 patients were found to have malignant polyps and were referred to Colorectal MDM. Of these 9 were diagnosed on biopsies while 8 were incidentally found after polypectomy.

The compliance rate of the CP-MDM outcomes was 82%.

61.6% in the therapeutic endoscopy group underwent the procedure in less than 8 weeks.

Conclusion: The CP-MDM is an innovative service achieved through a robust clinical governance framework for the management of complex polyps given the high compliance rate and single visit endoscopy therapy. An approved business case for a Pathologist to attend the CP-MDM regularly improves the multidisciplinary discussion of malignant appearing complex polyps and high grade dysplastic polyps.

References: Rutter MD, Chattree A, Barbour JA, et al. Gut Published Online doi:10.1136/gutjnl-2015-309576

Disclosure: Nothing to disclose

Poster presentations

Liver & biliary

Poster Presentations Liver & biliary

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Liver & biliary

09:00-19:00 / Poster Exhibition

P0829

NEW MARKERS OF NON-ALCOHOLIC FATTY LIVER DISEASE ON THE BACKGROUND OF METABOLIC SYNDROME

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Introduction: Modern pathogenesis of NAFLD has been associated with impaired regulation of cellular processes by microRNAs. MicroRNAs play one of the key roles in the post-transcriptional regulation of various pathophysiological processes in NAFLD. In recent years, there has been a growing body of evidence-based medicine and experimental studies demonstrating the regulatory role of microRNAs in the activation of more than 100 target genes involved in the pathogenesis of NAFLD. The most common of all the microRNAs presented in the liver are microRNA-122 and microRNA-34a. Although microRNAs play an important role in numerous metabolic and biological processes, the functions of most of the identified microRNAs remain unknown.

Aims & Methods: The purpose of the study was to study the expression levels of microRNA-34a, micro RNA-122 and determine their role in the development and progression of NAFLD on the background of metabolic syndrome.

Materials and methods. 78 patients with NAFLD combined with components of metabolic syndrome (MS), mean age 56.24 ± 10.9 years, were examined. The control group consisted of 30 healthy donors. Clinical examination of patients included evaluation of objective examination parameters, including anthropometric data, visceral adipose tissue (VAT) activity, and visceral obesity index (IVO) by the Amato M.C. method. For the diagnosis of non-alcoholic steatosis and liver fibrosis used an ultrasonic method of testing on the device "Soneus P7" (Ultrasign, Ukraine), with the function of elasto and steatometry with convex sensor 1-6 MHz. The expression of microRNA-34a and microRNA-122 was determined by sorption on NucleoSpinRmiRNA columns using a set of NucleoSpinRmiRNA plasma reagents (Macherey-Nagel, Germany).

Results: The level of relative normalized expression of microRNA-122 was significantly higher than that obtained for the expression of microRNA-34a and was 314.15 cu in the group of patients with NAFLD. vs. 2.98 cu in the control group. The expression of microRNA-122 in the plasma samples of patients with NAFLD compared to the control group was 105.4 times higher, as judged by the average relative expression of this microRNAs. When comparing the level of expression of microRNA-34a at different visceral adipose tissue activity, maximum values of the studied indicator were found in the group of patients with high IVO (184.92 cu), which was significantly different from the corresponding values in patients with low and moderate degree of VAT activity ($p < 0.05$). In patients with high-grade fibrosis, significantly high expression of microRNA-122 was observed. In the initial stages of fibrosis (F1-F2), there was also a moderate increase in the levels of the investigated microRNAs, which was trend-like but not significantly different ($p = 0.072$ and $p = 0.064$, respectively).

Conclusion: The levels of circulating microRNA-34a and microRNA-122 in the plasma samples of patients with NAFLD significantly exceeded those in the control group. Increased levels of microRNA-34a and microRNA-122 may be a potential marker of NAFLD development. A reliable association of microRNAs expression level with visceral adipose tissue activity was determined. MicroRNA-122 may act as a non-invasive marker of fibrosis progression in NAFLD patients with MS.

Disclosure: All authors have declared no conflicts of interest.

P0830

GUT-LIVER-AXIS: THE EFFECTS OF HEPATIC BARRIER (LIVER SINUSOIDAL ENDOTHELIAL CELL) AND NEUTROPHIL ON GUT-DERIVED LIVER INJURY

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Introduction: Liver diseases are associated with a leaky gut via the gut-liver-axis. Clinical observations suggest that inflammatory bowel disease (IBD) is usually manifested as damaged gut mucosa, but seldom leads to severe liver injury. Present reports indicate that the concomitant liver injuries in IBD patients are mostly nonalcoholic fatty liver disease (NAFLD) and drug-induced-liver-injury (DILI). Similarly, basic studies reveal that dextran sulfate sodium (DSS)-induced colitis does not lead to liver injury independently, but exacerbates existing liver diseases. These evidences raise the hypothesis that there is a "hepatic barrier" in the healthy liver, defending liver against gut-derived injury.

Aims & Methods: Since the liver is a large immune organ containing liver sinusoidal endothelial cell (LSEC) and various immunocytes, this study aims to identify which type of liver cell is the hepatic barrier in the gut-liver-axis. Seven liver disease models with different sorts of liver cell injuries were induced in SD rats: 1) sinusoidal obstruction syndrome (SOS, induced by crotonaldehyde), 2) liver cirrhosis (induced by CCl₄), 3) acute DILI (induced by CCl₄), 4) acute high-dose concanavalin-A (ConA) hepatitis, 5) acute low-dose ConA hepatitis, 6) chronic ConA hepatitis, and 7) NAFLD (fed by high-fat diet). Additionally, colitis was induced by 5% DSS in these 7 models to evaluate gut-derived liver injury. LSEC injury was evaluated by scanning and transmission electron microscope (SEM&TEM). Immunohistochemistry and flow cytometry were used to assess the changes of hepatic immunocytes. CXCL1 expression was tested by qRT-PCR. Neutrophils depletion was performed by injection of anti-rat-polymorphonuclear-granulocyte serum.

Results: Severe LSEC rupture was observed in the following 4 liver disease models: SOS, liver cirrhosis, DILI and acute high-dose ConA hepatitis, meanwhile DSS-colitis significantly aggravated liver damage of these 4 models. In contrast, DSS-colitis did not exacerbate liver damage when there was no LSEC injury in normal liver control, acute low-dose ConA hepatitis, chronic ConA hepatitis and NAFLD. Notably, LSEC was restored 3 days after modeling in DILI and acute high-dose ConA hepatitis, and colitis could no longer lead to liver damage thereafter. On the other hand, in SOS model, LSEC injury existed for at least 5 days, and liver injury could still be

enhanced by colitis. These results proved that colitis could aggravate liver injury only when LSEC was impaired, demonstrating the “hepatic barrier” role of LSEC in the gut-liver-axis.

For colitis-aggravated liver diseases above, massive neutrophils along with increased CXCL1 expression were observed in liver, while no significant changes were discovered for CD4⁺T cells, CD8⁺T cells, B cells and macrophages. We further depleted neutrophils in SOS and DILI, afterwards colitis could no longer aggravate hepatic injury. This result indicated that neutrophils might be a downstream effector in the mechanism of hepatic barrier.

Conclusion: Based on the results of various liver disease models in this study, LSEC is proven to play a key role as hepatic barrier in protecting liver against gut-derived injury. Neutrophils might be an important downstream effector in the development of colitis-aggravated liver damage. The mechanisms of LSEC as hepatic barrier and effect of neutrophils need to be further investigated.

Disclosure: Nothing to disclose

P0831

THE IMPACT OF RAMADAN FASTING ON FATTY LIVER DISEASE SEVERITY: A RETROSPECTIVE CASE CONTROL STUDY FROM THE HOLY LAND

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is emerging as an important public health condition. NAFLD spectrum ranges from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH) and cirrhosis. The effect of Ramadan fasting on several metabolic conditions such as body mass index [BMI] and lipid profile, and diabetes has been assessed.

Aims & Methods: The aim of the current study is to assess the impact of Ramadan fasting on NASH severity scores. A retrospective, case control study conducted in the Nazareth Hospital Between 2017 and 2019. The study population was divided in tow matched groups, one group represent NASH subjects who decided to fast all the Ramadan and the second group, control group, NAFLD/NASH subjects who decided not to fast. Metabolic/NASH severity scores, homeostatic model assessment of β -cell function and insulin resistance (HOMA-IR), NAFLD Fibrosis Score (NFS), BARD score and FIB4 score- all were assessed in both groups before and after the Ramadan month.

Results: 155 NASH subjects were included, 74 who fast and 81 subjects who decided not to fast. Among the fasting group, BMI decrease from 36.7 ± 7.1 to 34.5 ± 6.8 after fasting ($P = 0.003$), NFS decline from 0.45 ± 0.25 to 0.23 ± 0.21 ($P < 0.005$), BARD score declined from 2.3 ± 0.98 to 1.6 ± 1.01 ($P < 0.005$) and FIB4 score decline from 1.93 ± 0.76 to 1.34 ± 0.871 ($P < 0.005$). Moreover, HOMA-IR improved from 2.92 ± 1.22 to 2.15 ± 1.13 ($P < 0.005$).

Conclusion: Fasting improved on inflammatory markers, insulin sensitivity as well as in noninvasive measures for NASH severity assessment.

Disclosure: Nothing to disclose

P0832

FEATURES OF THE LEVEL OF HUMAN BETA-1-DEFENSIN IN PATIENTS WITH ALCOHOL-RELATED LIVER DISEASES

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Introduction: Human defensins, including beta-1-defensin (hBD-1) are considered as factors of nonspecific resistance of the body. The syndrome of bacterial overgrowth and bacterial translocation can lead to an increase in their activity in patients with cirrhosis. An increase in the level of hBD-1 may indicate the progression of the disease and is a predictor of the development of bacterial complications in patient with alcohol-related liver diseases (ALD).

Aims & Methods: Aim of the study is assessment of serum beta-1-defensin level in patients with alcohol-related liver diseases in correlation with clinical and laboratory datas of patients. 20 patients with alcoholic hepatitis and 39 patients with alcoholic cirrhosis were examined. 15 people entered the control group. Examination of patients included an assessment of the clinical picture of the disease, laboratory parameters (hematology, biochemistry, coagulation) and instrumental methods of investigation (ultrasound, gastroscopy). A liver biopsy was performed as indicated. The indices APRI, Forns, Fib4 were also evaluated to confirm liver fibrosis. The level of hBD-1 was determined by the ELISA method. The median, lower and upper quartiles (Me; LQ - UQ), and the correlation coefficient (r) were calculated.

Results: The study found that the level of hBD-1 in patients with alcoholic hepatitis ($779.0; 517.03-1285.02$ pg, $p < 0.001$) and patients with alcoholic liver cirrhosis ($630.1; 407.9-1003.2$ pg; $p < 0.05$) higher than in the control group ($419.8; 316.6-507.1$ pg). The level of hBD-1 was correlated with the severity class according to Child-Pugh ($r=0.42$), with Fib-4 ($r=0.4$), APRI ($r=0.46$); the degree of ascites ($r=0.44$), the degree of varicose veins of the esophagus ($r=0.36$), as well as the level of red blood cells ($r=-0.6$), hemoglobin ($r=-0.6$), platelets ($r=-0.4$), lymphocytes ($r=-0.53$), AST ($r=0.31$), creatinine ($r=0.54$), albumin ($r=-0.38$), direct bilirubin ($r=0.33$), de Ritis index ($r=0.34$) and prothrombin index ($r=-0.6$). The correlations of the level of beta-1-defensin indicate the relationship of this indicator with the progression of liver diseases. The development of fibrosis and cirrhosis of the liver leads to increased bacterial growth in the intestine and subsequently bacterial translocation. In turn, bacterial translocation stimulates the activation of factors of nonspecific resistance of the body. An increase in the activity of hBD-1 in patients with alcoholic hepatitis is associated with non-specific activation of the immune system due to chronic intoxication.

Conclusion: An increase in the concentration of beta-1-defensin in patients with alcoholic liver disease is associated with the activation of factors of nonspecific resistance of the body. This is due to the development of bacterial overgrowth syndrome and bacterial translocation, as well as the attachment of a bacterial infection.

Disclosure: The study was performed with funding from the Belarusian Republican Foundation of Fundamental Researches.

P0833

METHYLNALTREXONE AND RIFAXIMIN TREATMENTS SIGNIFICANTLY IMPROVE CHRONIC "LEAKY GUT" IN A DIET-INDUCED MOUSE MODEL OF NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Increased gut permeability ("leaky gut") occurs in the progression of numerous diseases, such as nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) and hepatic encephalopathy. These conditions are partially driven by proinflammatory bacterial products leaking from the gut into the bloodstream.

Aims & Methods: The aim of this study was to evaluate the mu-opioid receptor antagonist methylaltrexone and the nonsystemic antibiotic rifaximin for improving gut permeability in a diet-induced animal model of nonalcoholic fatty liver disease (DIAMOND), which develops chronic leaky gut and progressive NASH when fed a Western diet (WD). Four groups of 8 DIAMOND mice were initially fed a WD (Teklad 42% kcal from fat and 4% sugar water) for 8 weeks. Mice then continued on a WD and concomitantly received oral gavage administration of aqueous vehicle, methylaltrexone 50 mg/kg, rifaximin 400 mg/kg, or pioglitazone 30 mg/kg 5 times per week for 12 weeks (after ~4 weeks [Week 12], methylaltrexone and rifaximin doses were reduced to 25 mg/kg and 200 mg/kg, respectively). Gut permeability was assessed by a leaky gut assay at Weeks 12 and 20 by administering 4 kDa dextran 600 mg/kg orally followed by dextran quantitation in serum using a competitive enzyme-linked immunosorbent assay; increased gut permeability correlates positively with serum dextran concentration. Results between groups were compared using Student's 2-tailed t-test, and pair-wise analysis was performed on serial measurements at Weeks 12 and 20 to assess drug treatment effect on gut permeability.

Results: Mean serum dextran concentrations of vehicle WD mice at Week 12 (corresponding to NASH F0) averaged 166 mcg/mL. In the methylaltrexone group, mean serum dextran concentration at Week 12 (4 weeks of treatment) was 91 mcg/mL, a 1.8-fold reduction compared with the vehicle group ($P=0.04$). At Week 20 (12 weeks of treatment), compared with vehicle, mean serum dextran concentration was reduced by 2.9-fold with methylaltrexone ($P=0.01$) and 2.7-fold with rifaximin ($P=0.01$). Pioglitazone, the active comparator, also improved gut permeability vs vehicle at Week 20. By pair-wise analysis, rifaximin treatment continued improving the leaky gut induced by diet over time; Week 20 serum dextran in the rifaximin-treated group averaged 81 mcg/mL compared to the Week 12 average of 151 mcg/mL. Thus, rifaximin improved leaky gut by 46.2% in the 8 weeks between the first and second measurements ($P=0.05$).

Conclusion: This preclinical study showed that methylaltrexone and rifaximin treatments dramatically improved WD-induced gut permeability, suggesting that these compounds may have broad utility in treating inflammatory diseases exacerbated by "leaky gut." Further dose optimization studies are needed to determine if these compounds could be effective in NASH. These results support the biological rationale for further testing for efficacy in NASH, particularly in combination with drugs that target other mechanistic drivers of NASH, such as insulin sensitivity and inflammation.

References: N/A

Disclosure: Supported by Salix Pharmaceuticals. RC is a part owner and an employee of Sanyal Biotechnology LLC. WJ and ND are employees of Bausch Health Companies Inc or its affiliates and report being stock shareholders of Bausch Health Companies Inc. MB and JM are employees of Sanyal Biotechnology LLC.

P0834

FUNCTIONAL ACTIVITY OF BLOOD MONOCYTES IN PATIENTS WITH OPISTHORCHIS FELINEUS INFESTATION, DEPENDING ON THE SEVERITY OF LIVER FIBROSIS

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Introduction: Macrophages play a central role in the pathogenesis of chronic liver diseases and the possible development of fibrosis [1].

Aims & Methods: Aim : to study the activity of monocytes in patients with opisthorchiasis, depending on the severity of liver fibrosis.

A total of 74 patients with chronic opisthorchiasis (39 men and 35 women, average age 42.3 years) and 32 practically healthy patients (17 men and 15 women, average age 41.5 years) aged 24 to 60 years were examined. Opisthorchiasis was diagnosed by determining the eggs or bodies of adult parasites in duodenal contents and / or in the feces. Liver fibrosis was determined by elastometry according to the METAVIR scale in all 74 patients with opisthorchiasis. A study of the functional activity of monocytes in the blood was performed to all 74 patients with opisthorchiasis and 32 healthy individuals from the control group by chemiluminescent analysis with measuring the intensity of production of reactive oxygen species (ROS) in a spontaneous and zymosan-induced reaction in lucigenin- and luminol-dependent processes.

Results: METAVIR F2 liver fibrosis was registered in 20.3% of the examined individuals, METAVIR F3-F4 liver fibrosis was detected in 17.6% of patients with opisthorchiasis. A significant decrease in the functional activity of monocytes was registered in patients with opisthorchiasis in comparison with healthy individuals, as evidenced by a decrease in the maximum intensity of ROS production (Imax) and the area under the chemiluminescence curve (S) as in a spontaneous reaction (S was 403,200 ru versus 21,194,000 ru, $p < 0.001$), as well as in the zymosan-induced reaction (S was 2,077,000 ru versus 39,076,000 ru, $p < 0.001$). In the zymosan-induced reaction of the luminol-dependent process, in the spontaneous and in the zymosan-induced reaction of the lucigenin-dependent process, a decrease in S was observed in patients with METAVIR F3-F4 liver fibrosis in comparison with individuals with METAVIR F0-F1 liver fibrosis (Table).

Processes	Luminol-dependent			Lucigenin-dependent		
Stage of liver fibrosis by METAVIR	F0-F1 n=46 Me (Q25-Q75)	F3-F4 n=13 Me (Q25-Q75)	p	F0-F1 n=46 Me (Q25-Q75)	F3-F4 n=13 Me (Q25-Q75)	p
Maximum intensity of ROS production (Imax, r.u.) in spontaneous reaction	172 (61-565)	139 (70-789)	=0.7	122 (56-369)	91 (44-278)	=0.5
Area under the chemiluminescence curve (S, *1000 r.u.) in spontaneous reaction	468 (189-1,308)	299 (224-3,049)	=0.6	453 (227-1,235)	181 (79-768)	=0.04
Maximum intensity of ROS production (Imax, r.u.) in zymosan-induced reaction	660 (217-2,348)	164 (68-732)	=0.03	347 (91-1,032)	188 (59-768)	=0.2
Area under the chemiluminescence curve (S, *1000 r.u.) in zymosan-induced reaction	2,304 (956-6,596)	1,086 (327-4,561)	=0.02	1,131 (361-2,386)	345 (168-1,129)	=0.01

[Indicators of monocytes functional activity in patients with opisthorchiasis depending on the degree of liver fibrosis]

Conclusion: In patients with opisthorchiasis, METAVIR F3-F4 liver fibrosis

is associated with decreased functional activity of blood monocytes.

References: 1. Tacke F, Zimmermann HW. Macrophage heterogeneity in liver injury and fibrosis. *J Hepatol*. 2014;60(5):1090-6.

Disclosure: Nothing to disclose

P0835

SIGNALING OF THE NEUROPEPTIDE CALCITONIN GENE-RELATED PEPTIDE (CGRP) THROUGH RAMP1 PROMOTES LIVER FIBROSIS AND CONTROLS YES-ASSOCIATED PROTEIN (YAP) ACTIVITY DURING CHRONIC LIVER INJURY

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Introduction: Liver fibrosis is a repair response to chronic injury and a pathological process characterized by inflammation and accumulation of extracellular matrix. Advanced liver fibrosis can lead to cirrhosis, portal hypertension and eventually liver failure. Sensory nerves that innervate the liver secrete the neuropeptide calcitonin gene-related peptide (CGRP) which binds to the receptor activity-modifying protein (RAMP)1. Here, we investigate whether a deficiency of the neuropeptide receptor RAMP1 affects liver fibrosis upon chronic injury.

Aims & Methods: Wild type and RAMP1 deficient mice were injected with carbon tetrachloride (CCl₄) twice a week for four weeks to induce liver injury. The amount of CGRP receptor components in CCl₄-treated liver tissues was determined on RNA level by quantitative RT-PCR. The deposition of collagen fibers in the liver parenchyma was assessed by Sirius Red staining. The presence of fibrotic markers, including α-SMA and collagen, was assessed by Western blot analysis. Ki67-specific immunohistochemistry was used to quantify hepatocyte proliferation, and the regulatory components of the cell cycle were analyzed on protein and RNA levels. The influence of CGRP/RAMP1 on the Hippo pathway was tested by the presence of global or active YAP, as well as active YAP-regulators LATS1/2 and MOB1 using Western blot analysis. To investigate the effect of CGRP signaling on hepatic stellate cells, we stimulated the human hepatic stellate cell line (LX-2) in vitro with CGRP. α-SMA and the fibrotic marker collagen expression were quantified to analyze the activation of LX-2 cells after CGRP stimulation. Furthermore, YAP signal components were evaluated by detecting global and phosphorylated YAP proteins in LX-2 cells by Western blot analysis.

Results: Chronic liver injury induced by CCl₄-injection caused a sustained upregulation of hepatic CGRP mRNA and RAMP1 mRNA expression. In absence of RAMP1, murine livers turned out to possess less fibrosis as marked by decreased collagen fiber deposition. Livers of RAMP1 deficient mice showed lower expression of α-SMA and collagen type 1 proteins, indicating that CGRP/RAMP1 is critical for hepatic stellate cells activation. Absence of RAMP1 in CCl₄-treated mice led to a reduced hepatocyte proliferation, which is further verified by a diminished expression of cell cycle regulators on mRNA as well as protein level. Mechanistically, the expression of the Hippo pathway-regulated transcriptional coactivator YAP was decreased in livers of RAMP1-deficient mice following CCl₄ injection. Meanwhile, phosphorylation of YAP on Ser127, which promotes YAP inactivation through its cytoplasmic retention, was found to be elevated in RAMP1-deficient livers. Consistently, the phosphorylation of the YAP kinases LATS1/2 and MOB was upregulated. In vitro, the stimulation of LX-2 cells with the neuropeptide CGRP promotes the activation of hepatic stellate line cells and the synthesis of collagen 1a1 and collagen 1a2. In addition,

CGRP treatment resulted in YAP inactivation by its phosphorylation on Ser397 in LX-2 cells, which confirmed our in vivo results.

Conclusion: Our study shows that RAMP1/CGRP signaling promotes liver fibrosis and controls YAP activity, as well as the activation of LX-2 cells in vitro. The CGRP receptor RAMP1 can serve as a potential target of anti-fibrotic therapy for liver disease.

Disclosure: Nothing to disclose

P0836

COMPARISON OF STOOL MICROBIOTA, INTESTINAL PERMEABILITY AND SYSTEMIC INFLAMMATORY CYTOKINES IN NON ALCOHOLIC FATTY LIVER DISEASE AND ALCOHOLIC LIVER DISEASE

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Introduction: Alterations in gut microbiome have been described in non alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD). This is associated with increased intestinal permeability and systemic endotoxemia leading to liver injury and systemic inflammation. This plays a major role in pathogenesis of both ALD and NAFLD.

Aims & Methods: We conducted this study to assess and compare changes in gut microbiota, intestinal permeability and consequent systemic inflammatory markers in NASH and ALD patients. 36 NAFLD patients, 28 ALD patients and 21 controls with dyspepsia were included in the study. Stool microbiota analysis was performed in 10 patients in each group. DNA was extracted from stool samples and Nanopore sequencing was performed by using Oxford Nanopore MinION platform. NCBI 16S bacterial database was used to classify the reads. IL-6 and TNF-α were measured in serum by ELISA. Lactulose/Mannitol (L/M) ratio was calculated by NMR spectroscopy as a marker of intestinal permeability (I.P.).

Results: Bacteroides were increased in both ALD and NAFLD as compared to controls. Firmicutes abundance was decreased in both ALD and NAFLD. These changes were not statistically significant. Proteobacteria were increased in ALD and NAFLD as compared to controls and the difference was significant in ALD and controls. Firmicutes and Proteobacteria were increased in abundance in ALD as compared to NAFLD. At the genus level *Escherichia*, *Haemophilus*, *Streptococcus*, *Blautia*, *Bacteroides* and *Lactobacillus* were increased in ALD as compared to controls. Genus *Bacteroides*, *Prevotella* and *Escherichia* were increased in ALD as compared to NAFLD. Both ALD and NAFLD had a decrease in abundance of *Faecalibacterium* as compared to controls. Genus *Tyzerella*, *Oscillibacter*, *Ruminiclostridium*, *Oscillospiraceae*, *Megasphaera* and *Eubacteria* were significantly increased in abundance in NAFLD as compared to ALD. *Burkholderia* and *Intestinibacter* showed increased abundance in ALD as compared to NAFLD. There was a significant difference in I.P. as measured by L/M ratio between NAFLD and controls (0.0502(0.0208 - 9.071) and 0.0301(0.0102 - 1.238) respectively, p = 0.016). Though L/M ratio was increased in ALD - 0.0435(0.0177 - 1.435) this did not reach statistical significance. IL-6 was increased in NAFLD(57.30 (3.01 - 184.61)pg/ml) and ALD(58.190 (0 - 207.18) pg/ml) as compared to controls (13.61 (0 - 206.8 pg/ml) with a p value = 0.004. TNF-α was significantly increased in NAFLD(53.34(14.38 - 598.38)pg/ml) as compared to ALD(16.07 (6.95 - 188.54)pg/ml) and controls(12.33 (0 - 163.4)pg/ml), p < 0.001.

Conclusion: We demonstrated significant differences in intestinal microbiota composition among patients with NAFLD, ALD and control. There was difference in the stool microbiota between ALD and NAFLD with an increased abundance of SCFA producing bacteria in NAFLD. I.P. and sys-

temic inflammatory markers were increased in both ALD and NAFLD as compared to controls, though the change was significant only when comparing NAFLD and controls.

Disclosure: None

P0837

PREDICTIVE VALUE OF HEMATOLOGICAL PARAMETERS IN DETECTION OF SIGNIFICANT LIVER FIBROSIS

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Introduction: Parameters for a non-invasive assessment of the liver histology are constantly emerging. The association of parameters which are a part of standard complete blood counts (CBCs) and the histological outcomes of the liver diseases is widely investigated.

Aims & Methods: The aim was to analyse if hematological parameters of CBCs can be used as predictors of significant liver fibrosis, and to compare their predictive values to the ones of the standard liver fibrosis predictors. A retrospective study included a total of 260 patients who underwent liver biopsy. Based on the Metavir scoring system, patients were divided into two groups, those with no significant fibrosis (F0, F1; group 1), and those with advanced fibrosis and cirrhosis (F2, F3, F4; group 2). Hematological parameters, which included mean platelet volume (MPV), red-cell distribution width (RDW), platelet distribution width (PDW), MPV to platelet ratio (MPV/PLT), RDW to platelet ratio (RDW/PLT) and platelet count (PLT), were compared between the two groups. In those differing significantly, the aforementioned parameters and fibrosis degree were correlated. Receiver operator characteristics (ROC) curve analysis was conducted in those with significant results. ROC curves of evaluated hematological parameters and AST-platelet index (API), aspartate aminotransferase to platelet ratio index (APRI), and Fibrosis-4 (FIB-4) were compared.

Results: Differences between the two groups in MPV, RDW, MPV/PLT, PDW, PLT and RDW/PLT are presented in Table 1.

Variable	Group 1 (n=132)	Group 2 (n=128)	p-value
MPV (mean±SD)	9.08±1.3	9.17±1.22	0.579
RDW (mean±SD)	14.07±2.42	14.66±2.23	0.04
MPV/PLT (median, range)	0.04 (0.012-0.99)	0.05 (0.016-0.15)	0.001
PDW (median, range)	16.44 (10.0-59.2)	16.53 (13.3-55.5)	0.391
PLT (median, range)	202.55 (11.7-532)	167.5 (9.87-429.9)	<0.001
RDW/PLT (median, range)	0.067 (0.02-1.08)	0.081 (0.03-1.9)	<0.001

[Table 1. Differences between hematological parameters in the two groups.]

RDW showed a significant positive medium correlation with the fibrosis degree ($S=0.311$, $p<0.001$), while in the case of MPV/PLT and RDW/PLT correlation with the fibrosis degree was significant, positive, and weak ($S=0.234$, $S=0.237$ respectively, $p<0.001$). PLT expressed a significant negative weak correlation with the fibrosis degree ($S=-0.218$, $p<0.001$). PLT showed the highest sensitivity, (81.1%), but low specificity (44.5%), with a 150.7 cut-off value (COV), and the area under the curve (AUC) value of 0.62. MPV/PLT (AUC 0.62, COV 0.054), RDW/PLT (AUC 0.633, COV 0.079) and RDW (AUC 0.665, COV 13.96) had a sensitivity of 73.3%, 70.2% and 67.9% respectively, and a specificity of 54.1%, 54.7% and 62.5%, respectively.

Compared to the MPV/PLT, APRI and FIB-4 exhibited a significantly higher AUC in prediction of advanced fibrosis (0.62 vs. 0.697, $p=0.02$; 0.617 vs. 0.711, $p=0.005$, respectively). APRI and FIB-4 were superior in predicting fibrosis, compared to PLT (0.696 vs. 0.62, $p=0.01$; 0.697 vs. 0.617, $p=0.01$, respectively). FIB-4 showed a significantly higher AUC compared to RDW/PLT as well (0.695 vs. 0.628, $p=0.04$). No significant difference was observed between AUCs of RDW and standard indices, between MPV/PLT, RDW/PLT, PLT, and API, or between the RDW/PLT and APRI ($p>0.05$).

Conclusion: Based on our results, MPV/PLT, RDW, RDW/PLT, and PLT are not superior in determining the liver fibrosis compared to API, APRI, and FIB-4.

Disclosure: Nothing to disclose

P0838 WITHDRAWN

P0839

EFFECT OF BODY MASS INDEX ON THE RATIO OF THE MAIN MICROBIOTA PHYLOTYPES IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is currently the most common chronic liver disease in developed countries, and the number of patients with this pathology is growing rapidly. Today, there is no doubt the role of gut microbiota (GM) in the development and progression of NAFLD, including in patients with overweight.

Aims & Methods: To analyze the peculiarities of GM composition in patients with NAFLD depending on body mass index (BMI) in comparison with a group of apparently healthy people.

120 patients with NAFLD were examined (there were 59 men (49.2%) and 61 (50.8%) women among them) with an average age of 47 years. The first group consisted of 89 patients with identified concomitant obesity (OB) - BMI - 34.50 [31.50; 39.40], and the second group consisted of 31 overweight patients - BMI - 28.00 [27.20; 29.80]. In all patients, other causes of the development of secondary fatty liver dystrophy and factors affecting the state of GM were excluded. The control group consisted of 20 apparently healthy people: 8 men (40%) and 12 women (60%), with the average age of 43 years - BMI was 23.50 [21.30; 25.85]. Both groups were comparable in terms of gender and age. The study of the GM composition at the level of the main phylotypes was carried out by identifying the total bacterial DNA and *Bacteroidetes* (B), *Firmicutes* (F) and *Actinobacteria* (A) DNA, as well as the F/B ratio by the method of quantitative real time polymerase chain reaction (qRT-PCR) using universal primers for the 16S rRNA gene and taxon-specific primers. Statistical processing was carried out using the Statistica 13.1 package. Data are presented as Me [LQ; UQ], where Me is the median, LQ and UQ are the lower and upper quartiles, respectively.

Results: Patients with NAFLD and OB demonstrated statistically significant increase of F 52.12 [42.38; 67.39]% and F/B ratio 3.75 [1.7; 9.5] associated with significant decrease of B 13.41 [7.45; 26.07]%; in patients with NAFLD associated with overweight, relative quantity of F was 49.39 [37.47;

62.73]%, *F/B* ratio was 1.98 [1.15; 5.92], and *B* was 23.69 [12.11; 36.16]%. In individuals of the control group, the distribution of main GM phylotypes was essentially different, as the relative amount of *B* was almost the same as *F* 34.65 [24.58; 43.53]% and 29.97 [22.52; 41.75]%, and, respectively, the *F/B* ratio was 0.64 [0.52; 1.47]. At the same time, the relative amount of *A* showed almost no differences in either group - 5 [2.87; 9.14]%, 4.28 [1.53; 7.56]% and 5.47 [1.64; 12.79]%, respectively, and rather significant extent of other bacteria, which also had no statistically significant differences in the groups presented: 18.06[10.98; 28]%, 15.6[5.91; 26.26]% and 22.6 [16.0; 28.76]%, respectively.

Conclusion: Patients with NAFLD showed a progression in the severity of disorders in the quantitative composition of GM at the level of the main phylotypes due to an increase in the relative amount of *F* and the *F/B* ratio, which was directly proportional to the increase in BMI. These changes indicate a direct relationship between the GM composition and BMI in patients with NAFLD; a more profound change in GM in a larger number of patients may become the evidence base for the development of prognostic markers for early diagnosis of GM, identification of therapeutic targets and GM correction in patients with this pathology.

Disclosure: Nothing to disclose

P0840 WITHDRAWN

P0841

HEPATITIS B VACCINATION COVERAGE AMONG PHYSICIAN IN LEBANON

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Introduction: Hepatitis B virus (HBV) infection is a major global health. Health care workers (HCW) are at high risk for acquiring HBV. The WHO recommends the hepatitis B vaccine for adults at the highest risk of acquiring HBV infection. HBV vaccination coverage among HCWs shows a remarkable discrepancy worldwide.

The primary objective of the study is to determine the percentage of vaccinated, inappropriately vaccinated and unvaccinated physicians in Lebanon, and their distribution. The secondary objective is to determine the degree of testing for anti-HBs in physicians who received the hepatitis B vaccine.

Aims & Methods: It's a cross-sectional study over the period of 4 months, from December 2019 till March 2020; Attending Lebanese Physicians over the age of 30 years, and currently practicing in Lebanon were requested to fill out the questionnaire anonymously. The survey consisted of 18 questions, divided into multiple categories: demographical data including gender, age group, marital status, specialty and years of practice, hepatitis B vaccination status, screening for hepatitis B infection and immune status, availability of the vaccine at the workplace and the opinion regarding the hepatitis B vaccine,

Results: A total of 678 physicians were enrolled, 23.3% of Lebanese physicians were inappropriately vaccinated or non-vaccinated physicians and 76.7 % received the 3 hepatitis B vaccine doses (36.3% received a booster dose). 78.3% had a protective titer anti-HBs. 52% of physicians reported being exposed to blood products and 68% of participating physicians were never been screened for hepatitis B. 53% of physicians were offered the vaccine by the institutions where they practice, 90% of them find the vaccine mandatory for all physicians and 91% believe that there should be more awareness. 28.4% of male physicians being inadequately vaccinated

compared to 15.6% of female physicians ($p < 0.001$). No statistical significance in the vaccination status between physicians in the surgical versus non-surgical specialties. There was a statistically significant correlation between the vaccination status among physicians who were offered the vaccine, compared to those who were not.

Conclusion: There is a high number of unvaccinated physicians against the hepatitis B in Lebanon, warranting more education and awareness about the dangers of hepatitis B and the need for them to catch up on their vaccination status.

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Disclosure: Nothing to disclose

P0842

HEPATOCTE-TARGETED R-SPONDIN MIMETIC FOR LIVER REGENERATION

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Introduction: Wnt signaling plays a central role in hepatocyte expansion during development and tissue repair. R-spondins (RSPOs) amplify Wnt signaling via stabilization of Frizzled and LRP co-receptors and their function depends on the presence of Wnt ligands, which are upregulated in injured tissue. A major limitation to the potential therapeutic use of Wnts and RSPOs is their widespread effect on several organs, and in liver, on non-hepatocyte cells. To leverage the Wnt regenerative potential for parenchymal mass expansion, we generated a hepatocyte-targeted antibody-based R-spondin mimetic. We named this molecule, SWEETS-1, for Surrozen Wnt enhancer engineered for tissue specificity.

Aims & Methods: We tested the activity and specificity of SWEETS-1. *In vitro*, Wnt signaling activity was measured using the Huh-7 hepatic or HEK293 non-hepatic cell lines containing a luciferase gene controlled by a Wnt-responsive promoter (Super Top Flash reporter assay, STF). *In vivo*, SWEETS-1 (0.01-30 mg/kg), RSPO (0.01-10 mg/kg) or the negative control anti-beta-galactosidase (0.01-10 mg/kg) were injected intraperitoneally. Liver samples were collected 48 hours later for gene expression analysis of the Wnt target gene, *Axin2*, and for immunofluorescence analysis with the proliferation marker, Ki67 and the hepatocyte differentiation marker, HNF4-alpha. To examine the tissue-specific activity of SWEETS-1, expression of *Axin2*, was measured by qPCR in kidney, salivary gland, intestine, heart, lung, pancreas, skin and spleen.

Results: SWEETS-1 enhanced Wnt signaling in the Huh-7 hepatic cell line

to a level similar to that of RSPO. In contrast to RSPO, which induced Wnt signaling in the Huh-7 hepatic and HEK293 non-hepatic cell lines, SWEETS-1 activity was limited to Huh-7 cells. SWEETS-1 enhanced the expression of the Wnt target gene, *Axin 2*, to a level similar to that of RSPO. In contrast to RSPO which induced Wnt signaling in kidney, salivary gland, intestine, heart and pancreas, SWEETS-1 induced *Axin2* expression in liver only. Immunofluorescence analysis revealed that SWEETS-1 induced Ki67 positive nuclei specifically in HNF4-alpha-hepatocytes.

Conclusion: These results show that SWEETS-1 can stimulate hepatocyte-specific cell regeneration. This approach may be beneficial for the treatment of liver diseases.

Disclosure: All authors of past or current employees of Surrozen.

P0843

HEPATOCTE-TARGETED R-SPONDIN MIMETIC STIMULATES REGENERATION AND RESTORES COAGULATION IN A THIOACETAMIDE-INDUCED LIVER INJURY MODEL

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Introduction: Wnt signaling plays a central role in hepatocyte expansion during development and tissue repair. R-spondins (RSPOs) are known enhancers of Wnt signaling, via stabilization of Frizzled and LRP co-receptors. SWEETS-1 is hepatocyte-targeted R-spondin mimetic and antibody-based molecule, shown to specifically enhance Wnt signaling in hepatocytes both *in vitro* and *in vivo*.

Aims & Methods: We tested SWEETS-1 efficacy on hepatocyte expansion and liver function in a thioacetamide (TAA)-induced liver injury model. The TAA-induced liver toxicity mouse model was established by adding TAA in drinking water for 18 weeks. During the last 6 weeks of oral administration, TAA was injected intraperitoneally (i.p.) three times weekly. A control group, without TAA treatment, was included. Two days after discontinuing TAA treatment, mice were randomized based on body weights and INR values to SWEETS-1 (10 mg/kg) daily, a negative control, anti-GFP (10 mg/kg) twice weekly, or a positive control, RSPO (4.6 mg/kg) twice weekly for two weeks. As SWEETS-1 activity is dependent on the presence of Wnt ligands, we examined the expression of 17 Wnt ligands in TAA-treated and non-treated liver samples by qPCR and *in situ* hybridization. To examine the effect of SWEETS-1 on hepatocyte proliferation and maturation, proliferation markers were analyzed by qPCR, and immunofluorescence staining of Ki67 and HNF4-alpha, at days 3, 7 and 14. In addition, INR, clinical chemistry and histopathology were analyzed.

Results: Several Wnt family members, such as Wnt7b and Wnt9b, were elevated in TAA-injured livers, suggesting that SWEETS-1 could be efficacious in injured livers. Indeed, SWEETS-1 induced liver expression of the Wnt target gene, *Axin 2* to a level similar to that of RSPO. SWEETS-1 induced Ki67 positive nuclei, specifically in HNF4-alpha-hepatocytes, in TAA-treated mice. Furthermore, SWEETS-1 treatment restored TAA-impaired clotting time as measured by prolongation of INR to baseline levels. SWEETS-1 treatment did not induce any changes in AST or ALT.

Conclusion: These results show that the novel hepatocyte-targeted R-spondin mimetic, SWEETS-1, can stimulate hepatocyte-specific cell regeneration and that this effect reverses impaired coagulation. This approach may be beneficial for the treatment of acute or chronic liver diseases.

Disclosure: All authors are current or past employees of Surrozen.

P0844

INFLUENCE OF THE GUT MICROBIOME ON LIVER REGENERATION

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Introduction: Due to the high regenerative capacity of the adult liver, extensive partial resections of up to 75% are possible in patients as long as the remaining liver parenchyma is functional. However, postoperative liver failure poses a serious risk of mortality. The processes involved in liver regeneration, notably growth and control of hepatocyte proliferation, are still not fully understood. Recently, liver-extrinsic factors, particularly the gut microbiome and its derived metabolites, have increasingly been recognized as causal contributors to liver regeneration. Further, it was shown that important microbial readouts, such as the *Firmicutes/Bacteroidetes*-ratio, changes dramatically in animal models after partial hepatectomy. In our preliminary studies on mouse models, we could show that a large part of the lipid synthesis in hepatocytes relies on microbial metabolites from the large intestine. We therefore postulate that the gut microbiome provides factors via the portal vein that are necessary for the proliferation and growth of hepatocytes, such as short-chain fatty acids (SCFAs), and/or damage-associated molecular patterns (DAMPs).

Aims & Methods: The aim of this investigation was to experimentally test the importance of the gut-liver-axis, and in particular the intestinal microbiome in a preclinical mouse model. Partial liver resection (PHx) was performed in C57Bl/6 mice, whereby conventionally kept control animals (SPF) were compared with mice treated with germ-free animals and with animals that were re-colonized with an established minimal microbial consortium. The expression of proliferation markers was examined with qRT-PCR, the lipid synthesis using mass spectrometry, the tissue structure using immunohistochemistry on fixed tissue sections. All animals used were of the same age, sex, genetic background (B6) and feeding.

Results: While conventionally kept animals, as well as animals with defined microbial minimal flora, tolerated the PHx well and no mortality was observed, the germ-free mice from a gnotobiotic facility showed a highly significantly worse course after the intervention. The expression of enzymes in lipid synthesis and cell cycle markers was significantly reduced in the liver parenchyma of the germ-free animals.

Conclusion: The intestinal microbiome has a pronounced positive effect on liver regeneration in the preclinical animal model, presumably mediated by soluble microbial factors that enter the liver via the portal vein. We are currently recapitulating the experiment on animals treated with broad-spectrum antibiotics, as an orthogonal approach to determining the contribution of the microbiome.

Disclosure: Nothing to disclose

P0845

VISCERAL OBESITY AND ITS PROGNOSTIC VALUE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Visceral adipose tissue (VAT) is considered as a full-fledged metabolically active organ, which plays a significant role in the development and progression of a number of chronic diseases, such as non-alcoholic fatty liver disease (NAFLD), type 2 diabetes mellitus and a number of cardiovascular diseases. Therefore, the qualitative and quantitative determination of VAT indicators and their association with metabolic indicators is relevant and important from the point of view of the forecast.

Aims & Methods: Aim - to study the qualitative and quantitative parameters of VAT in patients with NAFLD and their association with metabolic parameters.

Object and research methods the main group - 85 patients with NAFLD, average age (52 ± 8.4) years. Control group 30 patients. Standard anthropometric parameters (body mass index (BMI), waist circumference (WT)), liver tests (alanine aminotransferase (ALT), asparaginaminotransferase (AST)), lipid parameters (total cholesterol (TCh), triglycerides (TG), low density lipoproteins were studied (LDL), high density lipoproteins (HDL), very low density lipoproteins (VLDL), atherogenicity coefficient (AC) and carbohydrate (fasting glycemia, glycosylated hemoglobin, HOMA - IR index) exchanges and their association with VAT. Quantitative indicators of visceral obesity (area of VAT, subcutaneous fat (SF), their ratio, sagittal diameter of the trunk (SDT) and the degree of steatosis was determined using computed tomography (CT). As an indicator of VAT dysfunction the visceral obesity index (VOI) was calculated according to the formula of Amato et al. (2015) [1].

Results: all examined patients of the main group had abdominal obesity (WC > 80 cm for women and WC > 94 cm for men). It should be noted that in 10% of women (n = 4) from the control group, WC indicators also exceeded 80 cm, however, they were not diagnosed with visceral obesity (the area of VAT did not exceed 130 cm² and IVO did not exceed 1 (0.74 (0, 66; 0.96) cu), which confirms the need to differentiate between the concepts of abdominal and visceral obesity (VO). 50% of the study group had a BMI > 30 kg / m², but the relationship between BMI and VAT is weak ($r = 0, 26, p < 0.05$). The area of VAT in patients of the main group averaged 186 (180; 189) cm², the coefficient of VAT / SF 0,8 (0,7; 0,9) U.mod, and ca the total body diameter was 27.7 (26.9; 28.9) cm, which is the criteria for the diagnosis of VO. VOI in patients of the main group was 3.7 (2.6; 5.6) undetected statistically significant direct the correlation between the indicators of VOI and ALT ($p < 0.05$), the area of VAT ($p < 0.05$), indicators of TCh, TG, VLDL ($p < 0.05$), indicators of Noma-IR ($p < 0.05$) and an inverse correlation with HDL indicators ($p < 0.05$). When distributing the patients of the main group according to the VOI indicators depending on the indicators of the radiological density of the liver, it was found that the degree of visceral fat dysfunction was associated with CT signs of severe liver steatosis (36 (34; 39) HU) ($r = 0.54, p < 0.05$).

Conclusion: The data obtained prove the significant role of visceral obesity as a prognostic marker for the development and progression of the degree of hepatic steatosis, dyslipidaemia and impaired carbohydrate metabolism. The study of the dynamics of qualitative and quantitative in-

dicators of visceral adipose tissue is relevant for the search for new therapeutic strategies and changes the plane of prognostic interpretation of the role of abdominal and visceral obesity.

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Disclosure: No conflict of interest

P0846

THE MODERN METHOD OF DIFFERENTIAL PURPOSE OF NON-DRUG TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE AND THE ROLE OF NUTRIGENETIC RESEARCH

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Introduction: The only recognized and effective method is non-drug treatment. Mediterranean diet has been identified as a priority because it contributes to the normalization of major metabolic parameters in patients with NAFLD. However, it is necessary to consider the possibilities of adherence to such a diet and the metabolic characteristics of patients in different regions of the world.

Aims & Methods: Objective: To study the nutrigenetic and nutritional parameters in patients with NAFLD.

Materials and methods. 85 patients (45 men and 40 women) with NAFLD were examined. All patients studied the features of eating disorders (ED) (DEBQ questionnaire), nutritional parameters - 5 polymorphisms: Pro-12Ala of the gene PPARG2 (rs1801282), 101027 gene of the ADRB2 gene (rs1042714) and Arg16Gly of the ADRB2 gene (1010282); (rs4994) and Thr54Ala of the FABP2 gene (rs1799883) associated with the risk of metabolic disorders.

Results: Two polymorphisms associated with ED gene disorders - Pro-12Ala PPARG2 and Trp64Arg ADRB3 - have been identified. No gender differences in the genotype frequency of the Pro12Ala polymorphism of the PPARG2 gene were detected ($p \times 2 = 0.90$). 84.4% of men and 82.5% of women were carriers of the PPARG2 gene polymorphism (OR = 1.10, CI = 0.24 - 4.99) of the Pro12Pro genotype (AB = 1.10, men and 16.7% of women of the genotype Pro12Ala (OR = 0.91, OR) = 0.20 - 4.13).

The distribution of genotypes and allelic variants of the ADRB3 gene polymorphism had significant differences ($p \times 2 = 0.05$). The Trp64Trp genotype of the ADRB3 gene polymorphism was detected in 80.0% of men and 55.0% of women, the Trp64Arg genotype in 20.0% of men and 32.5% of women, the Arg64Arg genotype was detected only in women. Analysis of the distribution of alleles 64Trp and 64Arg by sex using a multiplicative model showed that the reliability of the association of the minor female allele 64Arg is confirmed by a odds ratio of 3.13 (CI = 1.01 - 9.70) against 0.32 (CI = 0, 10 - 0.99) for the minor allele.

A reliable association ($p \times 2 = 0.02$) of the protective minor 12Ala allele with emotionally and restrictive types of ED (OR = 0.11, CI = 0.10 - 0.97) was established, whereas the external type of inclined ED was associated with the carrier of the main allele 12Pro polymorphism of the Pro12Ala PPARG2 gene (OR = 8.71, CI = 1.03 - 7.66). Analysis of the distribution of 64Trp and 64Arg alleles, depending on the type of EP disorder, showed a reliable association ($p \times 2 = 0.006$) of the metabolically unfavorable minor 64Arg allele

with the external type of ED disorders (OR = 5.53, CI = 1.48 - 20.68), whereas emotionally and restrictive types were associated with the main allele carrier 64Trp (OR = 0.18, CI = 0.05-0.68). In patients with NAFLD, an external type of ED disorder predominates ($p < 0.05$).

Conclusion: The association of ProARA2 polymorphisms of the PPARG2 gene and Trp64Arg of the ADRB3 gene have been established with malnutrition in patients with NAFLD. Thus, patients with NAFLD should be assigned an individual ED correction, taking into account the nutritional features identified that are associated with the risk of progression and development of complications of NAFLD.

Disclosure: Nothing to disclose

P0847

H63/H63D GENOTYPE AND THE H63D ALLELE ARE ASSOCIATED IN PATIENTS WITH HYPERFERRITINEMIA TO THE DEVELOPMENT OF METABOLIC SYNDROME

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Introduction: The metabolic syndrome (MtS) is present in the 25% of the population of Western countries. MtS is frequently associated with hyperferritinemia (HF) and this can be produced by mutations in the HFE gene. Mutations in the HFE gene, such as H63D / H63D, can be associated with MtS.

Aims & Methods: This was a prospective study including consecutive patients referred for HF (ferritin > 200µg / L women / > 300 µg / L men) from December 2010 to April 2013, which was designed to develop and validate a diagnostic algorithm for high iron overload based on laboratory and genetic variables (4).

We employed the Joint Interim Statement Criteria for MtS (International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity) (5). MtS was defined by the presence of three or more of the classical factors. DNA was extracted from the blood samples and HFE gene analysis was carried out by multiplex real-time PCR using LightCycler technology (LC 1.0).

Results: Out of 312 consecutive patients referred to our hospitals for HF, we had sufficient data to determine the MtS presence in 276. A total of 135 patients (49%), 115/240 men (48%), and 20/36 women (55.6%) presented metabolic syndrome.

HFE mutation analysis: In all patients with MtS (135) the mutations of the HFE gene were determined: wt / wt 41 (30.37%); C282Y/C282Y 1 (0.74%); C282Y/wt 7 (5.19%); H63D/H63D 21 (15.56%); H63D/wt 51 (37.78%); C282Y/H63D 8 (5.93%); S65C/wt 5 (3.70%); H63D/S65C 1 (0.74%). The genotypic frequency was compared with that of controls (general population) of the same region. The H63D/H63D mutation was 15.56% vs 3.70% in the control group ($p = 0.000$). The allelic frequency of the H63D mutation was 37.78% in the MtS group vs 20.37% in the control group ($p = 0.000$). The differences were statistically significant.

In a previous work from the same region the results were compared with a control group of blood donors from the same geographical area, but the patients were from Basque origin (Basque surnames in the last three

generations) (6). Considering the high percentage of H63D mutation in this populations-the highest in the world- (H63D/H63D 7.76%; H63D allele 31%), we have compared the results from the study with those of real general population in our country (8) and with those of Basque origin (6). When comparing with blood donors of Basque origin (6), the difference was nearly significant ($p=0.058$) (15.56% vs 7.76%). When we compared the results from the present study with those of real general population in our Country (8), the genotypic and allelic frequencies differences were statistically significant ($p=0.000$).

Conclusion: In conclusion, we can say from this study that the H63D/H63D genotype and the H63D allele are associated in patients with HF to the MtS in our country.

Disclosure: Nothing to disclose

P0848

SLEEVE GASTROPLASTY COMBINED WITH NLRP3 INFLAMMASOME INHIBITOR CY-09 REDUCE BODY WEIGHT, IMPROVE THE INSULIN RESISTANCE AND ALLEVIATE HEPATIC STEATOSIS IN MICE MODEL

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Introduction: Endoscopic sleeve gastropasty (ESG) has been suggested to be effective for treating obesity and its related non-alcoholic fatty liver disease (NAFLD). A small-molecule named CY-09 is the selective inhibitor of the NOD-like receptor pyrin domain-containing protein 3 (NLRP3).

Aims & Methods: To investigate whether a sleeve gastropasty surgery imitating ESG combined with CY-09 is more effective for treatment of obesity and NAFLD in mice model. Forty mice were randomly divided into a control group ($n=5$) and an NAFLD group ($n=35$) fed by high-fat diet (HFD). Then, the NAFLD mice were randomly assigned to the following groups at the time-point of 19 weeks: (1) sham surgery; (2) surgery; (3) the combination of surgery with CY-09 injection. NAFLD activity score (NAS) was used for histological evaluation of steatosis. We also detected fasting glucose and insulin to measure the homeostasis model assessment of insulin resistance (HOMA-IR).

Results: HFD resulted in significant obesity (45.0 ± 2.7 g vs. 29.4 ± 1.4 g, $P < 0.001$), metabolic disorder (HOMA-IR, 8.3 ± 1.0 mmol.mIU.L⁻² vs. 3.7 ± 1.0 mmol.mIU.L⁻², $P < 0.001$) and increased NAS (3.8 ± 0.8 vs. 0, $P = 0.01$), indicating successful modelling of NAFLD. The combination therapy resulted in a significantly lower body weight than the surgery alone at the end of the 8-week follow-up (40.4 ± 4.8 g vs. 45.0 ± 2.2 g, $P = 0.025$).

Furthermore, more dramatic improvements in HOMA-IR (5.8 ± 1.1 mmol.mIU.L⁻² vs. 12.2 ± 2.1 mmol.mIU.L⁻², $P = 0.036$) and NAS (4.5 ± 1.3 vs. 8.0 ± 1.8 , $P = 0.006$) were also observed in the combination group.

Conclusion: The surgery imitating ESG combined with CY-09 reduces body weight, improves insulin resistance and alleviates hepatic steatosis. The combination therapy may be a promising method for treating obesity and NAFLD.

Disclosure: Nothing to disclose

P0849

ASSOCIATION OF PRO12ALA POLYMORPHISM OF PEROXISOME PROLIFERATION ACTIVATOR RECEPTOR-GAMMA GENE WITH INSULIN RESISTANCE IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common nosology among hepatic diseases. According to the current data it covers 20-30% of the adult population in the countries of Western Europe and North America and 15% citizens in Asian countries. Insulin resistance is one of the leading etiologic factors for NAFLD development and considerable aspect that determines its progression.

Aims & Methods: The aim of the study was to investigate possible association of Pro12Ala polymorphism of peroxisome proliferation activator receptor-gamma (PPAR-gamma) gene with insulin resistance in NAFLD patients.

Pro12Ala polymorphism of *PPAR-gamma* gene was studied in 104 NAFLD patients (main group) and 45 healthy individuals (control group). The average age of patients was 55,2 ± 13,0 years, body mass index - 33,3 ± 5,3, 50 patients of the main group were men and 54 - women. The enrolled individuals of the control group were representative by age and gender distribution to those in the main group. NAFLD was diagnosed in accordance with EASL-EASD-EASO Guidelines (2016). Polymorphic variants of *PPAR-gamma* gene (Pro12Ala) rs 1801282 were determined. Biochemical blood parameters, insulin, leptin and adiponectin plasma levels were investigated. HOMA IR and J.F. Caro index were calculated in order to find out degree of insulin resistance. The study protocol was in accordance with the Helsinki Declaration (2013) and was approved by the local medical ethics committee. All patients and healthy individuals gave written informed agreement to participate in the study.

Results: Ala/Ala genotype of the *PPAR-gamma* gene was diagnosed in 2 individuals (1,9%), Pro/Ala genotype - in 28 (26,9%), Pro/Pro genotype - in 74 (71,2%) among NAFLD patients. In the group of healthy volunteers there were no homozygous carriers of Ala-allele, 9 persons (20,0%) from this group were heterozygotes, 36 (80,0%) - homozygous carriers of Pro-allele, which did not differ significantly from the genotypes distribution among NAFLD patients.

NAFLD patients Ala-allele carriers were found to have higher leptin level in the blood by 45,6 % (p = 0,04) as compared to Pro/Pro genotype carriers. Meanwhile adiponectin plasma concentration did not differ significantly between NAFLD patients with different *PPAR-gamma* genotypes. HOMA IR was elevated by 25,8% (p = 0,03) in NAFLD patients with Ala-allele of *PPAR-gamma* gene in comparison with those Pro/Pro genotype carriers. At the same time J.F. Caro index was decreased in 2,2 times (p = 0,02) in patients Ala-allele carriers as compared to those with Pro/Pro genotype. The above mentioned findings revealed cohort of NAFLD patients who are predisposed to more severe insulin resistance and thus to more inauspicious natural history of NAFLD.

Conclusion: NAFLD patients Ala-allele carriers of Pro12Ala polymorphism of *PPAR-gamma* gene are prone to elevated leptin in the blood and aggravated insulin resistance.

Disclosure: Nothing to disclose

P0850

NLRP3 INFLAMMASOME INHIBITOR CY-09 IMPROVES HEPATIC STEATOSIS IN EXPERIMENTAL NAFLD MICE

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Introduction: Non-alcoholic fatty liver disease (NAFLD) has become one of the most common chronic liver diseases and is estimated to be the leading cause of end-stage liver disease in the near future¹. One of the triggers for liver inflammation in pathogenesis of NAFLD has been identified as the NOD-like receptor protein 3 (NLRP3) inflammasome². A small-molecule named CY-09 is a new selective and direct inhibitor of the NLRP3 inflammasome, which has shown therapeutic effects on mouse models of type 2 diabetes³.

Aims & Methods: Whether CY-09 is effective for NAFLD in a high fat diet (HFD)-induced mouse model was investigated in this study. Twenty C57BL/6J mice were fed by HFD for 14 weeks, then randomly assigned into two groups: (1) a control group receiving 5% dimethylsulfoxide (DMSO) solution; (2) CY-09 group. In an 8-week follow-up, body weight, plasma total cholesterol (TC), plasma triglyceride (TG), plasma alanine transaminase (ALT), plasma aspartate transaminase (AST), oral glucose tolerance test (OGTT) and homeostasis model assessment of insulin resistance (HOMA-IR) were used to measure glucose metabolism. Liver steatosis was evaluated by gross morphology and NAFLD activity score (NAS).

Results: Except the sharp reduction on the first week, the weight of mice in DMSO group continued to increase and exceeded the initial weight on the 5th week of injection, while the gain of weight in CY-09 group was more stable, and was still slightly lower than initial weight at the end of study. The epididymal fat in CY-09 group was similar to that in DMSO group (2.35 ± 0.43 g vs. 2.20 ± 0.22g, P = 0.516). CY-09 significantly inhibited the elevation of TC (144.2 ± 7.6 mg/dL vs. 125.2 ± 12.3 mg/dL, P = 0.019), ALT (72.6 ± 16.7 U/L vs. 32.4 ± 2.7 U/L, P = 0.005) and AST (141.2 ± 11.8 U/L vs. 102.4 ± 9.3 U/L, P < 0.001), but increased blood TG content (54.4 ± 11.7 mg/dl vs 69.2 ± 3.7 mg/dL, P = 0.027). The area under the curve (AUC) of OGTT was less in CY-09 group (35.81 ± 6.79 mmol / L·hr vs. 22.91 ± 2.58 mmol / L·hr, P = 0.004), as well as HOMA-IR (14.36 ± 3.89 mmol.mIU.L⁻² vs. 8.82 ± 2.04 mmol.mIU.L⁻², P = 0.023).

Gross morphology showed that the livers of control mice were yellowish, while that of mice injected with CY-09 were normal in color. Microscopically, liver lipid droplets of CY-09 intervention mice were fewer and smaller with lower NAS (8.25 ± 1.26 vs. 3.20 ± 0.45, P < 0.001).

Conclusion: CY-09 is a potential drug for treatment of NAFLD. However, more researches on pharmacokinetics and pharmacodynamics is needed, as well as studies on the bioavailability of the human body, especially the liver, to prove whether it can be effectively applied to humans.

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Disclosure: Nothing to disclose

P0851

BILE ACIDS AND GUT MICROBIOTA IN THE PROGRESSION OF NON-ALCOHOLIC FATTY LIVER DISEASE AND HEPATIC CANCEROGENESIS

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Introduction: Nowadays, non-alcoholic fatty liver disease (NAFLD) is becoming one of the most frequent chronic liver diseases with outcome in fibrosis, cirrhosis and hepatocellular carcinoma (HCC). Assessment of the predictors of the progressive course of NAFLD is most relevant for studying the concentration of bile acids and gut microbiota.

Aims & Methods: Objective: To assess the impact of the bile acids composition, gut microbiota with development of fibrosis, cirrhosis, and HCC in NAFLD.

Methods: We examined 54 patients diagnosed with NAFLD, including 4 patients with HCC, 11 patients without fibrosis, 12 patients with fibrosis 1, 9 patients with fibrosis 2, 8 patients with fibrosis 3, 10 patients with cirrhosis. All patients underwent a laboratory/instrumental examination, including evaluation of the bile acids spectrum (cholic, deoxycholic, glycocholic, lithocholic, taurocholic, ursodeoxycholic), microbial markers in blood plasma using high-performance liquid chromatography combined with tandem mass-spectrometry. The degree of fibrosis was evaluated by elastometry. A statistically significant difference was evaluated using t-student test and Mann-Whitney test. To study the relationship between the variables, correlation and frequency analysis were used.

Results: The concentration of primary cholic acid in patients with F4 (84.4; 58.7 - 148.8) was significantly higher ($p < 0.001$) than: F0 (19.4; 11.6-35.1), F1 (16.3; 12.5 - 56.5), F2 (10.0; 5.2 - 17.4), F3 (15.5; 8.7 - 24.3). With HCC, the level of glycocholic acid (525.7; 267.1-1502.5) was higher ($p < 0.001$) than with F0 (30.7; 18.5 - 91.9), F1 (53.3; 41.7-127.5), F2 (31.9; 19.2 - 84.7), F3 (57.3; 30.2 - 108.4), taurocholic acid (2173.2; 903.8-3890.2) - than with F0 (72.5; 59.0-116.4), F1 (89.4; 73.1 - 167.3), F2 (83.7; 58.1 - 144.5), F3 (132.9; 85.3-248.1). The presence of fibrosis was inversely proportional to the concentration of ursodeoxycholic acid ($r = -0.9$; $p = 0.001$), Eubacterium lentum ($r = -0.6$; $p = 0.004$), Fusobacterium ($r = -0.6$; $p = 0.003$), Bifidobacterium ($r = -0.5$; $p = 0.027$), Propionibacterium ($r = -0.6$; $p = 0.006$), Cl. difficile ($p = -0.5$; $p = 0.016$), endotoxin ($r = -0.6$; $p = 0.003$) and is directly proportional to the level of Peptostreptococcus ($r = 0.8$; $p = 0.0001$), Bacillus megaterium ($r = 0.5$; $p = 0.025$).

Conclusion: The study found differences in the concentration of certain bile acids and microbial metabolites of the intestinal microbiota in patients with varying severity of liver fibrosis and HCC.

Disclosure: Nothing to disclose

P0852

BIOCHEMICAL CHARACTERISTICS OF CHILDREN'S BILE DEPENDING ON THE PRESENCE OF HEPATIC STEATOSIS AND TLR4 GENOTYPE

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Introduction: Recently, special attention has been paid to biochemical and genetic predictors of the non-alcoholic fatty liver disease in children. There is a variety of factors that can serve as triggers, among which the key role is played by bile acids in the bile.

Aims & Methods: Aim - to investigate the biochemical composition of bile in children, in dependence on the presence of liver steatosis and genotype TLR4

Materials and methods. At the Institute of Gastroenterology, 26 children were examined and divided into 2 groups: group 1 comprised 10 children with steatosis, group 2 consisted of 16 children without steatosis. The presence of liver steatosis was determined by using the apparatus "FibroScan502Touch" F60156 (Echosens, France) with the CAP test. The bile from patients was obtained by the method of duodenal sensing. The content of taurocholic (TC), taurodeoxycholic (TDC), glycocholic (GC) and glycodeoxycholic (GDC) bile acids in bile was determined by the thin layer chromatography method. The bile biochemistry was performed using conventional techniques. Children from both groups underwent molecular genetic testing in order to detect the SNP carriers of the TLR4 gene (Asp299Gly) in the "wild" (AA) or heterozygous (AG) state.

Results: 100% of the examined children with steatosis were found to be carriers of the "wild" genotype (Asp299Asp) TLR4 (AA), the bile (bile B) of these children showed a significant increase in cholic acid (CA) - 1.3 times ($p > 0.05$) as compared to group 2. It was remarked that the quantitative correlations of separate bile acid fractions tended to change: the TC content increased almost 2.5 times ($p > 0.05$), the GC content decreased 1.3 times ($p > 0.05$) accordingly, in comparison with group 2.

In group 1, changes in bile composition (bile B) occurred due to a 1.4-fold increase in the production of taurocholates in relation to glycocholates, with the simultaneous increase of the total amount of bile acids in the bile. In the children from group 2, the ratio of taurocholates to glycocholates was 1:2, the genetic feature of 12.5% of the children was the presence of the SNP gene TLR4 (Asp299Gly) in the heterozygous state (AG).

In children from group 1, the bile (bile C) content showed a significant increase in all fractions of bile acids: TC, TDC and GC - 1.3 times ($p > 0.05$), GDC - by 11% ($p > 0.05$), as compared to group 2.

Conclusion: Divergent changes have been established in the biochemical bile composition and in the correlations of bile acid fractions in the biles (B) and (C) in children with liver steatosis, being the carriers of the wild TLR4 genotype (Asp299Asp).

Disclosure: Nothing to disclose

P0853

EARLY KIDNEY DYSFUNCTION IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE - IS LIVER STIFFNESS MEASUREMENT USEFUL AS A SCREENING METHOD?

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Introduction: Increasing evidence suggests an association between non-alcoholic fatty liver disease (NAFLD) and chronic kidney disease. Timely prediction of early kidney dysfunction (EKD) promptly is thus essential in this population, although a screening method is not established.

Aims & Methods: **Aim:** to evaluate the role of transient elastography in predicting EKD in patients with NAFLD.

Methods: Prospective cohort study that included patients with NAFLD scheduled for evaluation, between May/2019 and January/2020. Demographic, clinical and laboratory data, and transient elastography (Fibroscan[®]) parameters were prospectively obtained. EKD was defined as microalbuminuria (urinary albumin-to-creatinine ratio 30-300mg/g) and estimated glomerular filtration rate ≥ 60 mL/min/1.73m². Liver fibrosis was defined as liver stiffness measurement ≥ 8.2 Kpa.

Results: Included 45 patients with NAFLD, 53.3% female gender, mean age of 53.5 $\pm$ 10.9 years. EKD was found in 17.8% of patients. NAFLD patients with EKD were significantly more obese (Body Mass Index ≥ 30) (75.0% vs 32.4%, $p=0.045$) and had significantly higher liver stiffness (8.5 $\pm$ 4.1 vs 5.8 $\pm$ 2.2 kPa, $p=0.01$) and hepatic steatosis levels in Fibroscan[®] (347.6 $\pm$ 43.6 vs 283.0 $\pm$ 69.1 dB/m, $p=0.02$). After multivariate analysis for adjustment of potential confounders for EKD including age, obesity, arterial hypertension and type 2 diabetes mellitus, the presence of liver fibrosis, remained a significantly predictor of EKD, being associated with a 14.2-fold increased risk of EKD ($p=0.04$).

Conclusion: Liver fibrosis is associated with a significant increased risk of EKD in patients with NAFLD, regardless of other comorbidities. Higher levels of liver stiffness, alert for timely identification of EKD and associated comorbidities, as well as their control, in order to prevent the development of chronic kidney disease in the long term.

Disclosure: Nothing to disclose

P0854

CPN-DC: IS THIS SCORE AN USEFUL TOOL IN THE SELECTION OF PATIENTS WITH CROHN'S DISEASE AND NAFLD?

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Introduction: Patients with Crohn's Disease (CD) have an increased risk of Non-Alcoholic Fatty Liver Disease (NAFLD) when compared with the general population. Apparently, factors such as chronic inflammation, surgery, drugs' hepatotoxicity, malnutrition and intestinal dysbiosis seem

to be involved in its pathogenesis. In 2020, the Clinical Prediction Tool for the NAFLD in Crohn's disease (CPN-CD) emerged and has a good accuracy for the identification of CD patients with NAFLD.

Aims & Methods: To assess the diagnostic yield of CPN-CD in predicting NAFLD in CD patients compared with the controlled attenuation parameter (CAP), assessed by the transient elastography (TE).

Retrospective study, which included CD patients that performed TE. The presence of NAFLD was defined as CAP > 288 db/m2 after excluding other liver diseases. CPN-CD was applied according to its original description, including variables such as age, gender, ethnicity, alanine aminotransferase (ALT), body mass index (BMI), diagnosis of cardiometabolic diseases, duration of CD and use of azathioprine or methotrexate.

Results: 103 patients were included, 54.4% female, mean age 38 $\pm$ 115 years, with mean disease duration of 92 $\pm$ 79 months. These patients presented an ileal/ileo-colonic/colonic distribution in 53.4%/36.9%/9.7% and an inflammatory/stricturing/penetrating phenotype in 44.7% / 34.0% / 21.4%, respectively. Of this population, 26.2% presented NAFLD. The mean value of CAP was 249 $\pm$ 58db / m2 and CPN-CD -0.54 $\pm$ 1.52.

CPN-CD presented an AUROC of 0.786 in predicting NAFLD. Scores of CPN-CD with a high probability of NAFLD ($> 50\%$) presented a sensitivity of 62.96%, specificity of 82.67%, a positive predictive value of 56.67% and a negative predictive value of 86.11%.

Conclusion: CPN-CD score presented a good accuracy in predicting NAFLD, with a good specificity. This tool is an asset in the selection of patients with CD who benefit a tight control of metabolic factors.

Disclosure: Nothing to disclose

P0855

NAFLD CV-RISK SCORE: A TOOL THAT ACCURATELY PREDICTS CARDIOVASCULAR EVENTS IN PATIENTS WITH NAFLD

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is associated with high cardiovascular morbi-mortality. The Framingham score was developed to predict the risk of cardiovascular events (CVE) in the general population, however, it does not include all parameters of the metabolic syndrome associated with CVE in patients with NAFLD. Recently, the NAFLD CV - Risk Score (NCVRS) was developed and validated, offering good accuracy in predicting the occurrence of CVE in patients with NAFLD. This score includes the mean platelet volume (MPV) that appears to be increased in patients with atherosclerotic disease and insulin resistance/NAFLD.

Aims & Methods: To assess and compare the diagnostic yield of the Framingham and NCVRS scores in predicting CVE. Retrospective study that included patients with NAFLD who underwent transient elastography (TE) with at least one year of follow-up. For each patient, the Framingham score and the NCVRS were calculated at the baseline.

Results: Included 96 patients with NAFLD, 66.7% female, with a mean age of 48.94 $\pm$ 12.9 years. We verify the occurrence of CVE in 14.4% of the patients during the follow-up. The mean BMI was 33.9 $\pm$ 6.5 kg/m2, MPV 10.29 $\pm$ 0.90, Framingham score 2.7 $\pm$ 4.19, NCVRS: -3.13 $\pm$ 1.24. Regarding TE values: CAP = 306.5 $\pm$ 46.65db / m2; E = 6.21 $\pm$ 2.63kpas.

The mean value of the NCVRS was higher in the group with CVE (-1.91 vs -3.34; $p < 0.001$). NCVRS presented an AUROC of 0.823 in predicting CVE. Long's method revealed, however, that the difference in AUROC from

NCVRS was not superior when compared to the isolated value of MPV (AUROC = 0.798; $p = 0.661$) and the Framingham score (AUROC = 0.713; $P = 0.137$). When applied the cut off > -3.98 defined by the authors, the NCVRS presented a sensitivity of 100%, specificity of 30.5%; PPV 19.7% and NPV 100% in predicting CVE.

Conclusion: NAFLD-CV score predicted with a good accuracy the occurrence of cardiovascular events, allowing an adequate identification of patients with NAFLD that may benefit from a timely optimization of metabolic factors.

Disclosure: Nothing to disclose

P0856

INCREASED ABUNDANCE OF *LACTOCOCCUS LACTIS* AS A FECAL BIOMARKER PREDICTING DEVELOPMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE AFTER FECAL MICROBIOTA TRANSPLANTATION IN HUMAN MICROBIOTA-ASSOCIATED RODENTS

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Introduction: Gut microbiota dysbiosis is increasingly linked to the development of non-alcoholic fatty liver disease (NAFLD). Whether this relationship is causal in nature has not been established. It is also uncertain whether certain gut microbiota signatures can predict the disease course of NAFLD. We aimed to address these issues via fecal microbiota transplantation (FMT) in a human microbiota-associated rodent model.

Aims & Methods: We recruited Asian human FMT donors categorized as three groups ($n=8$ each): obese NAFLD patients with body-mass index (BMI) ≥ 30 kg/m²; non-obese NAFLD with BMI < 25 kg/m²; and non-obese, non-diabetic healthy controls. NAFLD was diagnosed using controlled attenuation parameter (CAP) measurements via transient elastography (Fibroscan, Echoscans, Paris), with steatosis defined as CAP ≥ 248 dB/m.

After antibiotic administration, collected human fecal samples were transplanted individually without pooling to the same number of C57BL/6J mice, categorized as FMT-obese, FMT-lean and FMT-healthy. We collected liver, adipose tissue and blood from mice after a 12-week high-fat diet for assessment of histology, lipid metabolism, hepatic inflammation and intestinal barrier function. We performed shotgun metagenomics sequencing using the Illumina Novaseq 6000 platform and analyzed microbiome from the collected fecal samples.

Results: Obese NAFLD human donors, when compared to non-obese NAFLD and healthy controls, had a significantly higher mean CAP (355.9 $\pm$ 9.6 dB/m vs. 299.3 $\pm$ 8.9 dB/m vs. 186.3 $\pm$ 11.2 dB/m; $p=0.01$) and mean BMI (34.4 $\pm$ 1.6 kg/m² vs. 23.7 $\pm$ 0.4 kg/m² vs. 20.7 $\pm$ 0.8 kg/m²; $p<0.001$).

Principal coordinates analysis of microbiota profile at the phylum level based on Bray-Curtis distance showed non-obese NAFLD donors had a significantly more distinct gut microbiota composition compared with healthy controls ($p=0.0341$) and obese NAFLD donors ($p=0.0479$). FMT-healthy mice, when compared to FMT-obese mice, had significantly lower plasma triglyceride levels (110.0 $\pm$ 7.115 mg/dl vs. 207.9 $\pm$ 11.52 mg/dl, $p<0.0001$), significantly lower intrahepatic triglyceride content (48.80 $\pm$ 4.463 mg/g vs. 68.51 $\pm$ 4.183 mg/g, $p=0.0061$); decreased hepatic lipid accumulation (Oil Red O stained lipid droplets: 9.709% $\pm$ 3.231% vs. 21.37% $\pm$ 4.312%, $p=0.0483$); and decreased adipocyte size (10914 $\pm$ 1437

μm^2 vs. 18455 $\pm$ 2267 μm^2 , $p=0.0045$). Tight junction protein zonula occludens-1 (ZO-1), an intestinal barrier marker, was significantly upregulated in FMT-healthy when compared to FMT-obese (1.370 $\pm$ 0.4163 vs. 0.3302 $\pm$ 0.1272, $p=0.0316$). There was no statistical difference in the above-mentioned results when comparing FMT-healthy vs. FMT-lean ($p>0.05$ for all).

Linear Discriminant Analysis Effect Size plot of taxonomic biomarkers showed a greater abundance of *Lactococcus lactis* in FMT-healthy mice when compared to FMT-obese mice (43.50% $\pm$ 12.92% vs. 24.82% $\pm$ 12.76%, FDR- $p=0.044$). *Lactococcus lactis* correlated positively with tricarboxylic acid cycle pathway, a major energy-producing pathway involved in triglyceride breakdown ($\rho=0.59$, $p=0.002$), but correlated negatively with plasma triglyceride levels ($\rho=-0.45$, $p=0.027$).

Conclusion: In this human microbiota-associated rodent model, FMT from healthy human donors prevented the development of NAFLD in mice, signifying a potentially causal relationship. The fecal presence of *Lactococcus lactis* as a biomarker was associated with a reduced risk of NAFLD development. Future animal and human interventional studies will be required to determine the feasibility of *Lactococcus lactis* as a therapeutic option for NAFLD.

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Disclosure: Nothing to disclose

P0857

FIBROSCAN-AST (FAST) SCORE: WHICH PATIENTS ARE AT HIGHER RISK ACCORDING TO THE NEW DIAGNOSTIC TOOL ON NON-ALCOHOLIC FATTY LIVER DISEASE?

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is an increasingly prevalent cause of chronic hepatic disease. In 2020, the Fibroscan-AST (FAST) score was internationally validated, a new score that aims to identify patients with non-alcoholic steatohepatitis at higher risk of progression to cirrhosis, based on transient elastography (TE) findings and serum levels of aspartate aminotransferase (AST).

Aims & Methods: We aimed to identify, in patients with NAFLD, which metabolic syndrome (MS) conditions may predict a higher FAST-score and subsequently a higher risk of progression to cirrhosis. We conducted a retrospective study of consecutive patients with NAFLD submitted to TE between January 2016 and December 2019. Patients without an AST serum sample collected within 6 months of the TE were excluded. FAST-score was calculated, stratifying the patient's risk as low (< 0.35), medium (0.34-0.67) or high (> 0.67).

Results: The sample included 132 patients, 52.3% of the female gender, with a mean age of 52 years. FAST-score presented a significant moderate correlation with *Fib4* ($r=0.558$; $p<0.01$).

On univariate analysis, patients with *Diabetes mellitus* (DM) ($p<0.01$), dyslipidemia ($p=0.025$) and smoking habits ($p=0.01$) presented with significantly higher FAST-scores. Additionally, patients with 3 components of MS presented higher scores when compared to those with 2 or less components ($p<0.01$).

Smoking ($p=0.035$) and DM ($p<0.01$) kept significant results when adjusted for confounding factor in multivariate analysis. DM patients had not only a higher score, but also a higher percentage of cases in the high-risk group ($p<0.01$).

Conclusion: Calculating the FAST-score, patients with NAFLD and DM and/or smoking habits presented with a higher risk of progression to cirrhosis, with that risk being simultaneously higher in the presence of at least 3 components of the MS. In the presence of the comorbidities stated above, patients with NAFLD should be precociously referred to specialized consultation, assuring a correct risk stratification and optimization of therapeutic approach.

Disclosure: Nothing to disclose

P0858

SERUM MALONDIALDEHYDE IS ASSOCIATED WITH NON-ALCOHOLIC FATTY LIVER AND RELATED LIVER DAMAGE DIFFERENTIALLY IN MEN AND WOMEN

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Introduction: Non-alcoholic fatty liver disease (NAFLD) and steatohepatitis (NASH) are associated with increased oxidative stress and lipid peroxidation. However, no large studies tested the association of oxidative damage of lipids with human NAFLD and NASH, thoroughly adjusting for metabolic and lifestyle risk factors.

Aims & Methods: The aim of the current study was to test the association of malondialdehyde (MDA), as a marker of oxidative damage of lipids, with NAFLD and liver damage markers, and to test the association between dietary vitamins E and C intake and MDA levels. This was a cross-sectional study among subjects who underwent blood tests including FibroMax for non-invasive assessment of NASH and fibrosis. MDA was evaluated by reaction with Thiobarbituric acid and HPLC-fluorescence detection method. Food-frequency questionnaire was used to evaluate nutritional intake. Fatty liver was diagnosed by abdominal ultrasound.

Results: MDA measurements were available for 394 subjects. In multivariate analysis, the odds for NAFLD were higher with the rise of MDA levels in a dose-response manner, adjusting for age, gender, BMI, and lifestyle factors. Only among men, higher serum MDA was associated of higher odds for NAFLD and NASH and/or fibrosis (OR= 2.59, 95%CI 1.33-5.07, $P=0.005$; OR= 2.04, 1.02-4.06, $P=0.043$, respectively). The upper tertile of vitamin E intake was associated with lower odds of high serum MDA level (OR=0.28 95%CI 0.13-0.62, $P=0.002$).

Conclusion: Serum MDA is associated with NAFLD and markers of NASH or fibrosis among men. Dietary vitamin E intake is inversely related with MDA levels, suggesting a pathway for its protective role in NASH.

Disclosure: Nothing to disclose

P0859

METABOLIC PROFILE OF PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE. A SINGLE CENTER EXPERIENCE

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is related to obesity, insulin resistance and other parameters of the metabolic syndrome. However, obesity has been suggested to be associated with NAFLD in the absence of other metabolic disorders.

Aims & Methods: The aim of the study was to assess the clinical and laboratory metabolic profile in patients with NAFLD. The medical charts of NAFLD patients referred to our outpatients' clinic because of abnormal liver biochemistry and/or the presence of fatty liver were thoroughly reviewed. Metabolically healthy people were defined those who met none of the following criteria: BP $\geq 130/85$ mmHg or under hypertension treatment, fasting glucose ≥ 100 mg/dl or under diabetes treatment, serum triglycerides > 150 mg/dl, HDL cholesterol $< 40/50$ mg/dl for men/women.

Results: The medical charts of 569 NAFLD patients were initially retrieved; 250 patients were excluded because of other chronic liver diseases (hepatitis B, hepatitis C, autoimmune hepatitis and hemochromatosis). Finally, the study included 319 patients [(M/F: 161/152), mean age of diagnosis 51.41 years (16-84)]. Twenty-one (6.6%) patients were metabolically healthy [3 (14.3%) normal weight (BMI < 25), 10 (47.6%) overweight (BMI 25-29.9), 8 (38.1%) obese (BMI > 30)]. Mean ALT concentration was 73.42 IU/L (range 13-414), mean AST concentration was 47.75 IU/L (range 11-240), and mean γ GT concentration was 55.42 IU/L (range 11-280). Metabolically healthy participants were significantly younger ($p<0.001$) and had significantly lower levels of serum γ GT ($p=0.009$) compared to metabolically unhealthy participants. In contrast, no significant differences were observed between the two groups in serum AST, ALT, INR and total bilirubin levels. In a similar way, metabolically unhealthy patients did not present a significantly higher risk of cirrhosis (RR=1.02, $p=0.978$) compared to metabolically healthy participants.

Conclusion: The majority of the metabolically healthy participants in our study were overweight / obese. Metabolically healthy NAFLD patients were younger compared to metabolically unhealthy, although the risk of cirrhosis was similar between the two groups. These findings suggest that metabolically healthy fatty liver may be an early stage of metabolic syndrome development.

Disclosure: Nothing to disclose

P0860

INCREASED RISK OF METABOLIC-ASSOCIATED FATTY LIVER DISEASE AND ADVANCED FIBROSIS IN INFLAMMATORY BOWEL DISEASE INDEPENDENT OF CLASSIC METABOLIC RISK FACTORS

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Introduction: Increased risk of metabolic-associated fatty liver disease and liver fibrosis in inflammatory bowel disease independent of classic metabolic risk factors.

Aims & Methods: The aim of this study was to determine the prevalence and risk factors of MAFLD in IBD patients.

Methods: cross sectional, case control study including all recorded IBD patients above 18 years old attended at the IBD outpatient consultation of the University Hospital Marques de Valdecilla in Santander (Spain). Controls were age, gender, type 2 diabetes (T2D) and BMI-matched in a 1:2 ratio and came from a general population random sample. MAFLD was established by controlled attenuation parameter (CAP) measured with transient elastography (TE) with a threshold of 248 db/m. Liver fibrosis was estimated by liver stiffness measurement (LSM) with TE and liver biopsies were obtained when significant liver fibrosis was suspected (LSM>7.2 kPa with M probe or >6.2 kPa with XL probe).

Results: From a total of 880 IBD patients and 1792 controls evaluated, 831 IBD and 1718 controls fulfilled the inclusion criteria and were included in the study. MAFLD was diagnosed in 349 IBD patients (41.99%) and 563 controls (32.77%) ($p<0.001$), being the diagnosis of IBD an independent predictor of MAFLD from classic metabolic risk factor (adjusted OR 1.99; $p<0.001$). Despite cases and controls were BMI and T2D-matched, both obesity and T2D were underrepresented in IBD-MAFLD patients compared to MAFLD in the general population. LSM was significantly higher in IBD compared to controls, and in MAFLD associated to IBD compared to MAFLD in the general population. IBD constitutes an independent risk factor for advanced LSM (>8.7 kPa) (Adjusted OR 4.63; $p<0.001$), together with male gender, obesity and T2D. The prevalence of advanced LSM is higher in Crohn's disease (CD) compared to ulcerative colitis (UC) (27/166 [16.3%] compared to 15/174 [8.6%]; $p=0.005$), being CD an independent predictor of advanced LSM in IBD-MAFLD population. Liver biopsy was obtained in 35 out of 100 IBD patients with suspected presence of MAFLD with significant fibrosis. MAFLD diagnosis was confirmed in all cases and the presence of any degree of fibrosis (F1-4) in 24/35 (68.6%) and advanced fibrosis (F3-F4) in 5/35 (14.3%).

Conclusion: Our results show a higher prevalence of MAFLD and liver fibrosis in IBD patients independent of classic metabolic risk factors. To the best of our knowledge, this is the first study with biopsy-proven MAFLD to show this association. At the light of these results, the awareness of a concomitant presence of MAFLD in IBD patients should be encouraged.

Disclosure: Nothing to disclose

P0861

IS EXCHANGEABLE COPPER, A BETTER PROGNOSTIC TOOL FOR ASSESSING TREATMENT CONTROL IN HEPATIC WILSON'S DISEASE IN CHILDREN?

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Introduction: Standard assessment of chelation adequacy in Wilson Disease (WD) by liver function test (LFT), non-ceruloplasmin copper (NCC) and 24- hour urine copper (UCu) has fallacies. Exchangeable copper (ExCu) is a newer concept in the diagnosis and management of neurological WD.

Aims & Methods: The aim of the study is to explore the role of ExCu as a prognostic tool for assessment of therapy in liver disease. Hepatic WD patients on ≥ 1 y chelation therapy was prospectively enrolled. Newly diagnosed chelation-naïve WD children were controls. ExCu in ultrafiltrates was analysed by atomic mass spectrophotometry. REC was defined as percentage ratio of ExCu and total serum copper. Sub-group analysis of ExCu on degree of chelation [well-chelated (UCu 200-500 $\mu\text{g/day}$); poorly chelated (UCu < 200 or >500 $\mu\text{g/day}$)] and liver disease [stable (normal liver synthetic function and transaminases < 2 times upper limit normal) and unstable (poor synthetic functions and elevated transaminases)]

Results: 96 children ($n=61$ on chelation, $n=35$ controls) aged 12.5 ± 4.4 y were assessed. Chelated WD vs. controls had lower ExCu (0.9 ± 0.6 vs 3 ± 7 $\mu\text{mol/L}$, $p=0.03$) and higher REC ($43 \pm 27.4\%$ vs $30.4 \pm 14.3\%$, $p=0.01$). Table 1 shows the differences with respect to chelation status and liver disease. AUROC of ExCu in chelated vs. controls was 0.8 (cut-off 0.97 $\mu\text{mol/L}$, sensitivity 80%, specificity of 68%, $p<0.01$) and stable vs. unstable liver disease was 0.73 (cut-off 0.87 $\mu\text{mol/L}$, sensitivity 77%, specificity of 65% $p=0.01$). ExCu had positive correlation with NCC ($r=0.92$, $p<0.001$), UCu ($r=0.52$, $p<0.001$) and Pediatric end-stage liver disease (PELD) scores ($r=0.47$, $p=0.01$).

Multivariate analysis of the entire cohort showed Child Turcotte Pugh scores ($p=0.002$) and duration of treatment (> 1-year vs < 1-year) ($p=0.002$) significantly influences ExCu values. Median follow-up duration was 10 (0-24) months. 14/96 (15%) of the entire cohort either died or were referred for liver transplantation. Survival on Kaplan Meier curves were significantly higher ($p=0.01$) if baseline ExCu was ≤ 0.87

Patients characteristics	Well chelated (n= 53)	Poorly chelated (n= 8)	p value	Stable liver disease (n= 48)	Unstable liver disease (n= 13)	p value
PELD score	-2.53 ± 5.6	-5.57 ± 2.2	0.166	-4.17 ± 4.3	1.77 ± 6.4	<0.001
Serum ceruloplasmin (mg/dl)	6.79 ± 6.2	5.52 ± 3.2	0.603	5.9 ± 5.5	8.67 ± 7.8	0.15
Non-ceruloplasmin copper ($\mu\text{mol/L}$)	-0.17 ± 2.6	5.51 ± 3.45	<0.001	0.59 ± 3.4	0.32 ± 2.5	0.79
24 h urinary copper ($\mu\text{g/day}$)	342.7 ± 82.3	643.4 ± 633.7	<0.001	484.96 ± 340.3	422.10 ± 432.8	0.59
Exchangeable copper ($\mu\text{mol/L}$)	0.95 ± 0.5	1.01 ± 0.7	0.795	0.86 ± 0.5	1.3 ± 0.6	0.01
Relative exchangeable copper (%)	47.3 ± 26.7	12.04 ± 5.3	<0.001	41.95 ± 27.7	47.11 ± 27.1	0.53

[Comparison between chelation status and liver disease ($n=61$)]

Conclusion: Exchangeable copper is an effective monitoring tool to assess chelation. New chelators require ExCu levels to reduce to $>0.97 \mu\text{mol/L}$ for 1 year and thereafter achieve liver stability if values are $<0.87 \mu\text{mol/L}$.
Disclosure: Nothing to disclose

P0862

BURDEN AND COSTS OF NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN PORTUGAL

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is currently recognized as one of the leading causes of chronic liver disease related to the increased prevalence of obesity and metabolic syndrome. It is thought to affect 25% of the adult global population and 17% of the Portuguese population. Despite NAFLD being common, benign and reversible, a small proportion of patients will develop non-alcoholic steatohepatitis (NASH). NASH can progress to the whole spectrum of disease severity from advanced fibrosis to cirrhosis, hepatocellular carcinoma and the need for liver transplants.

Aims & Methods: This study aimed to estimate the cost and disease burden associated with NAFLD and its progression in 2017 mainland Portugal. A population-based multiple cohort model was designed to estimate the distribution of the prevalence of the different disease progression states based on cumulative disease incidence over time. Disease burden was measured as disability adjusted life years (DALYs). Costs to the healthcare system were also estimated. Incidence and prevalence of NAFLD in Portugal were retrieved from a population-based study (E-COR) *.

Results: Adjusted prevalence of NAFLD was 17.0%, in 2017. During this year, there were 55 deaths attributed to NASH that resulted in the loss of 952 years of life lost (YLL). A total of 50 years lived with disability (YLD) were attributable to NASH. The total disease burden was 1002 DALY. The estimated direct cost attributable to NAFLD progression in 2017 was approximately 61 million €.

Conclusion: The total burden attributable to NAFLD is quite low, compared to other diseases such as heart failure or hypercholesterolemia. However, NAFLD is frequently associated with metabolic comorbidities including obesity, insulin resistance and type 2 diabetes, which makes people with NAFLD a high-risk group. Studies investigating NAFLD should include other comorbidities associated with complex and dynamic diseases to capture its full impact beyond liver diseases.

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P0863

GENERAL PRACTITIONER DATABASE NAFLD (GPS-NAFLD) STUDY: PREVALENCE OF ADVANCED LIVER FIBROSIS AMONG ITALIAN PRIMARY CARE PATIENTS WITH NAFLD

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is now the most prevalent liver disease in the world. Its prevalence varies from 20 to 28% in adults. NAFLD involves a spectrum of conditions from simple steatosis to steatohepatitis (NASH) and fibrosis. Liver fibrosis is considered as an integral part in the progression of chronic liver disease ultimately leading to cirrhosis and hepatocellular carcinoma.

Aims & Methods: This study aimed at assessing the prevalence of advanced liver fibrosis among Italian primary care patients with NAFLD/NASH. Data were extracted from Health Search database (HSD) of the Italian College of General Practitioners and Primary Care. Patients' demographic data were linked by an encrypted code to clinical records, drug prescriptions, specialist referrals, and hospitalization. Liver fibrosis was evaluated by the Fibrosis-4 Index (FIB-4). Patients were divided in two groups: younger and older than 65 years. FIB-4 cutoffs of 2.67 or 3.25 were used to identify advanced liver fibrosis for the younger than 65 years while for the older was used a cutoff of 2.

Results: HSD provided data for 918,954 patients registered in the primary care services. In total 151,431 cases of NAFLD/NASH were identified. Diabetes was present in 37,413 (24.71%) cases. Among 113551 cases with available BMI, 42,314 (37.26%) were considered obese. FIB-4 data were available in 3,723 (4.4%) cases of whom 1,715 (46.1%) were older than 65 years. The mean FIB-4 score was 1.1 ± 2.0 in the younger group and 1.9 ± 2.2 for those older 65 years. The prevalence of advanced fibrosis was 27.5% [95% CI, 25.47- 29.76] in the elderly. In the younger group for the cutoffs of 2.67 and 3.25 the prevalence was 2.74 % [95% CI, 2.07- 3.55] and 1.64% [95% CI, 1.13- 2.30] respectively. Considering both cutoffs for the younger group, the prevalence was however smaller than for those older than 65.

Conclusion: HSD consultation allows the first primary-care record study in Italy to assess the prevalence and stratification of NAFLD patients with liver fibrosis. Improving the identification of advanced fibrosis in NAFLD presence is of major importance for the clinical decision-making and helps detecting patients who will benefit from risk factor modification or personalized approach to contrast further progression to cardiovascular and/or hepatic complications.

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P0864

ULTRA-PROCESSED FOOD INTAKE IS ASSOCIATED WITH FEATURES OF METABOLIC SYNDROME AND LIVER DAMAGE

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Introduction: Ultra processed foods (UPF) are characterized by lower nutritional quality, high energy density and presence of additives and widespread in Western diets. High consumption of UPF was recently associated with all-cause mortality and cancer, in few studies also with metabolic syndrome (Mets), but not with non-alcoholic fatty liver disease or steatohepatitis (NAFLD or NASH).

Aims & Methods: The aim of this study was to test the association of UPF consumption, with Mets and its components and with liver damage. This was a cross-sectional study among subjects who underwent anthropometric and blood pressure measurements and blood tests including FibroMax for non-invasive assessment of NASH and fibrosis. Fatty liver was diagnosed by abdominal ultrasound. Mets was diagnosed according to the acceptable criteria. Food-frequency questionnaire was used to evaluate UPF consumption using the NOVA classification. High UPF intake considered as UPF Kcal/total Kcal intake above the sample median, corresponding to 28%, 28.4% among the entire sample or subjects with NAFLD, respectively.

Results: 789 subjects included in the total sample, reliable FibroMax test was obtained from 714 subjects. 305 subjects diagnosed with NAFLD. In multivariate analysis adjusting for age, gender, body mass index, energy intake and other nutritional habits, high consumption of UPF was significantly associated with higher odds for Mets (OR=1.85, 95%CI 1.28-2.69, P=0.001) and its components hypertension, high TG and low LDL (OR=1.53, 95%CI 1.05-2.21; P=0.026; OR=1.63, 1.09-2.44, P=0.017; OR=1.46, 1.04-2.06, P=0.031, respectively) among the entire sample and with higher odds for NASH and hypertension (OR=1.81, 95%CI 1.01-3.24, P=0.047; OR=2.14, 1.13-4.08, P=0.020, respectively) among subjects with NAFLD.

Conclusion: High UPF consumption is associated with Mets, and among NAFLD subjects with NASH and hypertension, factors that indicate more severe state. Thus, decrease of UPF intake may be effective to prevent NAFLD deterioration.

Disclosure: Nothing to disclose

P0865

NUTRITIONAL PATTERNS OF PATIENTS WITH NAFLD SIGNIFICANTLY DIFFER TO THOSE IN A CONTROL GROUP

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Introduction: Nutritional assessment with the use of food patterns allows to evaluate the structure of foods and products consumed and to analyse which group of products have greater impact on the disease development and progression.

However, little is known about food patterns in Russian patients with non-alcoholic fatty liver disease (NAFLD) [1].

Aims & Methods: **Aim:** to evaluate nutritional patterns in patients with NAFLD in comparison to the control group without the disease.

Materials and Methods: Blinded to patients' personal details retrospective database search for unique records of patients aged 18-75 y.o. with complete data about their demography, nutritional assessment with the use of food frequency method was performed in Nutrilogic database (LLC Nutrilogic, Russia). These patients should have had no mention of food intolerance/allergies, history of major abdominal surgery, and disorders or conditions (including alcohol abuse or use of some medications), that have a potential to trigger fatty liver disease. The obtained group was analysed for the presence of codes or statement of non-alcoholic fatty liver disease in the diagnosis (NASH, simple steatosis, NAFLD) and divided to NAFLD (in case the condition was present) and the control group (no mention of the disease). Nutritional patterns were assessed in accordance to "healthy eating pyramid" principles for the following main groups of products: grains, fruits, vegetables, dairy products, meats, fats and confectioneries. Non-parametric statistics was used to perform the comparison of the main and the control group.

Results: Data of 251 with NAFLD and 62 controls were available for the final analysis.

Comparison of the main food groups' consumption revealed larger amounts of intake of dairy products and meats in NAFLD group compared to control.

	NAFLD, n=251	Control, n=62	p
Grains*	1.16±0.88	1.04±0.51	0.658
Vegetables*	1.39±1.0	1.15±0.99	0.177
Fruits*	0.77±0.63	0.82±0.62	0.551
Dairy products*	0.84±0.78	0.39±0.31	0.001
Fats*	0.78±0.63	0.68±0.59	0.254
Confectioneries*	0.34±0.39	0.25±0.28	0.263
Meats*	2.18±1.68	1.44±0.77	0.002

The data are shown in accordance to the normative values of consumption of food and products in the ration of specific calorific value according to the concept of the „pyramid of healthy nutrition” [2].

[Table 1. Pattern of consumption of main food products in the studied groups]

The structure of vegetables consumption in patients with NAFLD differed from the controls. They consumed more potatoes (0.15±0.20 vs 0.07±0.09, p=0.001), onions (0.06±0.09 vs 0.05±0.10, p=0.006), and cabbage (0.14±0.17 vs 0.11±0.21, p=0.005), then controls. However, the structure of beans, root crops, leafy and other vegetables consumption did not differ between the groups. Patients with NAFLD eat more fruits and fruit products, containing larger amounts of sugars: melons (0.06±0.19 vs 0.02±0.08 in the control group, p=0.001), citrus (0.11±0.15 vs 0.10±0.17, p=0.001). The structure of fats consumption significantly differed by animal fats (0.10±0.30 in NAFLD, 0.008±0.02 in the control group, p=0.001) but did not differ by rates of vegetable oils, margarines and dairy butter consumption.

Conclusion: Nutritional patterns of patients with NAFLD and the control group differ significantly. The obtained data may be used for diet modification in patients with NAFLD.

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P0866

ESTIMATED ANNUAL LIVER GROWTH PREDICTS NEED FOR TREATMENT IN POLYCYSTIC LIVER DISEASE

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Introduction: Polycystic liver disease (PLD) is characterized by growth of hepatic cysts that can lead to hepatomegaly in autosomal dominant polycystic liver disease or kidney disease (ADPLD/ADPKD). Treatment (either surgical or drug therapy) is only required in symptomatic patients. The prognosis of PLD is variable, ranging from stable disease to gross hepatomegaly.

Aims & Methods: We evaluated whether cross-sectionally determined hepatic growth rate predicts the probability of treatment in PLD. We estimated annual growth rates of polycystic livers in adult PLD patients from the international PLD-registry using liver volumetry on baseline CT or MRI-scans. Height-corrected total liver volumes (hTLV) were calculated and patients that received treatment before scan were excluded. We used 902.25 mL/m at 18 years as a starting point for liver volume. We divided the growth rates (rounded to 1 decimal) in tertiles ordered from slowest to fastest growth. Baseline characteristics included age, sex, treatment center, diagnosis (ADPKD/ADPLD). The primary outcome was occurrence of treatment for PLD after baseline imaging grouped as: 1. no treatment 2. minimally invasive treatment (drug therapy, cyst fenestration or aspiration sclerotherapy) and 3. invasive treatment (segmental hepatic resection, liver transplantation). Statistical analyses were performed with Kruskal Wallis and chi-squared tests. We used a Cox proportional hazards regression model to adjust for confounders.

Results: We included 1179 patients, with a median follow-up time of 53 months (IQR: 33-84). Estimated annual growth rates in the tertiles were divided as $\leq 0.1\%$ /year for the lowest tertile (slow, n=431), 0.1 to 1.6%/year for the middle tertile (intermediate, n=369) and $> 1.6\%$ /year for the highest tertile (fast, n=379). Compared to intermediate and slow growth, patients with fast growth had a significantly higher hTLV at baseline (median: 2533 vs 1122 vs 794 mL; $P < 0.001$), were more frequently female (76.5% vs 51.2% vs 57.3%; $P < 0.001$) and ADPLD was more often the underlying diagnosis (15.6% vs 7.0% vs 2.6%; $P < 0.001$).

The proportion of treated patients increased with each tertile (3.2% vs 17.6% vs 47.2%; $P < 0.001$). In patients with slow growth, 3.2% received minimally invasive and 0.0% invasive treatment. With intermediate growth, 17.3% underwent minimally invasive and 0.3% invasive treatment. The highest treatment rates were seen with fast growth as 35.3% received minimally invasive and 11.9% invasive treatment.

After adjusting for sex, diagnosis and treatment center, Cox regression analysis showed increased probability for overall treatment (either minimally invasive or invasive) for intermediate compared to slow growth (hazard ratio (HR) 2.3; CI 1.3-4.2; $P = 0.005$) and fast compared to slow growth (HR 2.1; CI 1.2-3.7; $P = 0.012$). Treatment probability did not increase for fast compared to intermediate growth (HR 0.9; CI 0.7-1.2; $P = 0.492$). However, the probability for invasive treatment was higher in fast compared to intermediate growth (HR 18.9; CI 2.5-142.9; $P = 0.004$).

Conclusion: Estimated annual liver growth using baseline liver volume accurately predicts the probability of treatment in PLD patients. Invasive procedures occurred almost exclusively with fast growth ($> 1.7\%$ /

year), while treatment (invasive or minimally invasive) was rare with slow growth ($< 0.1\%$ /year). This study provides the basis for evidence-based clinical counseling of PLD patients regarding prognosis.

Disclosure: Nothing to disclose

P0867

SERUM MIR-421 AND LNCRNA MEG3 AS BIOMARKERS FOR THE DIAGNOSIS OF NON-ALCOHOLIC FATTY LIVER DISEASE IN CHILDREN

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Introduction: Early detection of NAFLD in children has priority for the prevention of disease progression. In last years circulating microRNAs (miR) and long non-coding RNAs (lncRNAs) have been proposed as novel biomarkers for NAFLD and NASH.

Aims & Methods: Our study aimed to examine differences in miR-421 and lncRNA maternally expressed gene 3 (MEG3) expression levels between children with NAFLD and obesity and to investigate the association of transcriptome markers with anthropometric, immunological and liver structure parameters. The study was conducted on 66 children aged 6-17 years. Liver steatosis was evaluated via transient elastography with controlled attenuation parameter (CAP) measurement (Fibroscan®, Echosens, France). According to CAP, body mass index levels patients were divided into 3 groups: 1 group - 29 children with NAFLD, 2 group - 30 children with obesity/overweight, 3 group (control) - 7 children with normal weight. The levels of miR-421 and lncRNA MEG3 in serum samples were explored via qRT-PCR. Cytokine profile was studied by the evaluation of IL-6, IL-10 and TNF- α levels with enzyme immunoassay. The relationship between miR-421, MEG3 levels and clinicopathological features in NAFLD was investigated.

Results: Significantly increased levels of miR-421 and lncRNA MEG3 were observed in obese children (14.5 ± 3.9 ; 110.2 ± 27.3 , respectively, $p < 0.05$) and NAFLD patients (45.9 ± 16.3 ; 145.9 ± 21.4 , respectively, $p < 0.05$). Serum miR-421 and MEG3 levels clearly correlated with body mass index ($r = 0.367$; $r = 0.383$, respectively, $p = 0.01$), waist circumference ($r = 0.374$; $r = 0.386$, respectively, $p = 0.01$), CAP ($r = 0.416$; $r = 0.386$, respectively, $p = 0.01$) in NAFLD patients. Also, serum miR-421 concentration was positively correlated with TNF- α and TNF- α /IL-10 ratio levels ($r = 0.421$; $r = 0.375$, respectively, $p = 0.01$).

Conclusion: Thus, our results demonstrate that serum levels of miR-421 and lncRNA MEG3 changed in one direction and were significantly up-regulated in obese children and NAFLD patients. Circulating miR-421 and lncRNA MEG3 correlated with anthropometric data and proinflammatory cytokine, so might be promising diagnostic biomarkers of NAFLD in children.

Disclosure: Nothing to disclose

P0868

PREDICTORS OF ADVANCED FIBROSIS IN NAFLD: ONE MORE STEP TOWARDS NONINVASIVE ASSESSMENT

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a very frequent and overall benign condition. However, a proportion of patients develop progressive disease with liver fibrosis and cirrhosis. So far, the gold standard to determine the presence of parenchymal inflammation and fibrosis is liver biopsy, an invasive and not risk-free method. Since liver fibrosis is the most important prognostic factor in NAFLD and it correlates with liver-related outcomes and mortality, great efforts have been made in order to develop non-invasive and accurate methods that can determine the presence of liver fibrosis in these patients.

Aims & Methods: We conducted a retrospective single-center study in our tertiary care hospital, including all patients from January 2018 to December 2019 that performed liver stiffness evaluation by transient elastography (TE) with FibroScan® for NAFLD non-invasive staging. All patients were diagnosed with NAFLD by clinical, laboratorial, imaging methods and/or liver biopsy. Patients with excessive alcohol consumption (>140g/week in women and 210g/week in men) and other causes of liver diseases were excluded.

Data pertaining this population was considered valid if obtained in a period no longer than 6 months from liver stiffness evaluation by TE. We registered sex, age, body mass index (BMI), personal history of diabetes, dyslipidemia, hypertension, cardiac and/or cerebrovascular disease, platelet count, aspartate aminotransferase, alanine aminotransferase (ALT), gamma-glutamyltransferase, albumin, total bilirubin and international normalized ratio. We considered low grade fibrosis (F0-F2) if liver stiffness < 8 KPa and high grade fibrosis (F3-F4) as liver stiffness ≥ 8 KPa.

Our aim was to identify independent clinical predictors of advanced liver fibrosis, as evaluated by TE. Subsequently, we developed a score to further identify these patients.

Results: We included 154 patients, 57.1% were males, with an average age of 54.84±12.31 years.

The most common comorbidities were dyslipidemia (64.3%), hypertension (53.2%) and obesity (IMC >30: 52.6%). Average liver stiffness was 8.79 kPa, with 59.1% of patients having low grade fibrosis (F0-F2).

Univariate analysis was performed, followed by logistic regression, and the following variables were independently associated with advanced fibrosis: ALT levels ≥ 42 (OR 3.66), female sex (OR 3.08), diabetes (OR 2.33), age > 55 years (OR 2.20) and obesity (OR 2.01).

A score was built based on this model and points were attributed according to the odds ratio calculated (4, 3, 2, 2 and 2 point to ALT, female sex, diabetes, age and obesity, respectively) to a maximum score of 13 points. This model accurately predicted the presence of advanced fibrosis in our group of patients (p < 0.001, AUROC 0.774). A cut-off point of ≥ 5 points was considered to be optimal and selected for our model, as it provided a sensitivity of 90.5%, specificity of 51.7%, positive predictive value of 56.4% and negative predictive value of 88.7%.

Conclusion: In our population, this model was able to accurately identify patients with advanced fibrosis. Most importantly, it enabled to rule-out advanced fibrosis (F3-F4) with 88.7% certainty in patients with NAFLD, when a cut-off of ≥ 5 points was utilized.

By applying this score in our cohort, we could identify the group of patients without advanced fibrosis that could probably have been safely referred for follow up in primary care.

With further validation in a prospective study, this simple model could be an useful tool in clinical practice, in order to stratify the prognosis of NAFLD patients.

Disclosure: Nothing to disclose

P0869

ANALYSIS OF RISK FACTORS FOR NONALCOHOLIC STEATOHEPATITIS IN OBESE CHILDREN: A CASE-CONTROL STUDY

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide. Nonalcoholic steatohepatitis (NASH) is one of the inauspicious forms of NAFLD, associated with progression of the disease.

Aims & Methods: Our study aimed to investigate the role of clinical and anamnestic factors in NASH development prediction in children. A case-control study was conducted on 170 children aged 6-17 years, 90 children (53%) had NAFLD, 37 (41%) children among them had NASH. Liver steatosis was evaluated via transient elastography with CAP measurement (Fibroscan). We used logistic regression to estimate adjusted odds ratios (ORs) with 95% confident intervals (CIs) for incidence of NASH. Potential risk factors for NASH were evaluated considering age, sex. Also, χ^2 test was used to compare demographic characteristics between the two groups.

Results: Univariate analysis showed that risk factors for NASH were male sex, maternal obesity, birth weight more than 4.0 kg, obesity, abdominal type of fat distribution, metabolic syndrome, small intestine bacterial overgrowth, biliary sludge. According to the results obtained from multivariate logistic regression analysis, the adjusted OR (95% CI) for NASH was 1.62 (1.30-1.90), including male sex (OR=1.41, 95% CI 1.16-2.07), metabolic syndrome (OR=2.95, 95% CI 1.29-6.78), maternal obesity (OR=1.54, 95% CI 1.16-2.07), birth weight more than 4.0 kg (OR=1.31, 95% CI 1.17-1.95), small intestine bacterial overgrowth (OR=1.48, 95% CI 1.20-2.20), biliary sludge (OR=1.34, 95% CI 1.14-1.82) (p < 0.05).

Conclusion: The results suggested that anamnestic factors such as birth weight, existence of maternal obesity, male sex and clinical signs such as presence of metabolic syndrome, small intestine bacterial overgrowth and biliary sludge are the risk factors for NASH development in children.

Disclosure: Nothing to disclose

P0870

SERUM CYTOKERATIN-18 LEVELS IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE AND OBESITY

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Introduction: In the last decades scientific attention has been focused on non-alcoholic fatty liver disease progression prediction. Serum cytokeratin-18 (CK18) is considered as a novel serological marker for the diagnosis of steatosis/fibrosis in NAFLD patients.

Aims & Methods: Our study aimed to evaluate the cytokeratin-18 (CK18) levels in children with non-alcoholic fatty liver disease (NAFLD) and obesity and to investigate its relation to liver and vascular structure characteristics and biochemical parameters. The survey included 158 patients aged 6 to 17 years with an average age of patients ($12,15 \pm 2,51$) years. Determination of liver steatosis was carried out with “FibroScan502Touch” (Echosens, France) and controlled attenuation parameter (CAP) measurement. According to CAP, alanine aminotransferase, body mass index levels and the presence of overweight / obesity patients were divided into 4 groups: 1 group - 34 patients with non-alcoholic steatohepatitis (NASH), 2 group - 48 patients with simple steatosis (NAFLD), 3 group - 61 patients with overweight / obesity without liver steatosis, 4 group (control) - 15 patients with normal weight without liver steatosis. Serum CK18 concentration was quantified with enzyme immunoassay (IDL Biotech AB, Sweden). Pearson’s chi-square correlation analysis were used to examine the associations between CK18 and various parameters.

Results: Serum CK18 was significantly higher in the NASH group (97,2 (91,8; 142,1) U/l) versus the NAFLD group (59,5 (46,3; 105,1) U/l), obese patients (49,9 (40,5; 70,4) U/l) and the control group (59,2 (57,6; 63,7) U/l) ($p < 0,05$). Correlation was established in NASH group between CK-18 and total cholesterol ($r = 0,627$; $p < 0,05$), low-density lipoproteins ($r = 0,755$; $p = 0,007$), carotid intima-media thickness ($r = 0,9$; $p < 0,05$), liver stiffness (according to transient elastography) ($r = 0,389$, $p < 0,05$) and CAP ($r = 0,774$; $p < 0,001$). In NAFLD patients CK18 correlated with carotid intima-media thickness ($r = 0,881$; $p < 0,01$) and liver steatosis ($r = 0,504$; $p < 0,05$).

Conclusion: Significantly elevated serum CK18 was observed in NASH patients in comparison with NAFLD patients and obese children. In addition, CK18 level was significantly associated with lipid metabolism parameters, carotid intima media thickness and steatosis/fibrosis degree in children with NASH.

Disclosure: Nothing to disclose

P0871

STEATDIAB A SCORE FOR IDENTIFYING TYPE 2 DIABETES MELLITUS PATIENTS AT RISK FOR DEVELOPING MODERATE STEATOSIS

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Introduction: The prevalence of nonalcoholic fatty liver disease (NAFLD) is increasing proportionately with the increasing of obesity and type 2 diabetes. It is known that liver steatosis is a risk factor for developing liver fibrosis in type 2 diabetes patients together with other metabolic factors.

Aims & Methods: The aim of this study was to identify risk factors associated with moderate steatosis and to develop a score that could be used in daily practice.

A prospective study on 536 patients with type 2 diabetes was conducted. We aimed for 10 valid CAP and liver stiffness measurements (LSM). To discriminate between fibrosis stages, we used the following VCTE cut-offs: $F \geq 2 - 8.2$ kPa, $F \geq 3 - 9.7$ kPa, and $F4 - 13.6$ kPa [1]. To discriminate between steatosis stages, we used the following CAP cut-offs: S1 (mild) - 274 dB/m, S2 (moderate) - 290dB/m, S3 (severe) - 302dB/m [1]. For developing a score for stratifying the risk of moderate steatosis, we used univariate and multivariate regression analysis.

Results: Out of 536 patients, 23.6% patients had no steatosis, 9.1% patients had mild steatosis (S1), 6.9% patients had moderate steatosis (S2), while 60.4% had severe steatosis (S3).

In univariate analysis, female gender ($p = 0.01$), BMI ($p < 0.0001$), waist circumference ($p < 0.0001$), elevated levels of AST ($p = 0.007$), total cholesterol, HDLc ($p < 0.0001$) triglycerides ($p = 0.01$), blood glucose ($p = 0.003$), fibrat treatment ($p = 0.01$), presence of hypertension ($p = 0.01$) were associated with at least moderate steatosis. The STEATDIAB score is composed by: 1 point for high BMI (> 25 kg/m²), presence of hypertension, waist circumference (greater than 100 cm), blood glucose (greater than 200 mg/dl), cholesterol (greater than 300 mg/dl), triglycerides (greater than 250 mg/dl), HDLc (less than 35 mg/dl), AST (greater than 124 U/L), fibrat treatment. The maximum score can be 9 points. The cut-off value for identifying patients at risk for developing moderate steatosis is 5 points, AUROC = 0.77, 95% CI (0.71-0.82).

Conclusion: Type 2 diabetes patients with more than 5 points at STEATDIAB score are at risk for developing moderate steatosis.

References: Eddowes P, Sasso M, Allison M et al. Accuracy of FibroScan Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. *Gastroenterology*. 2019;156(6):1717-1730. doi:10.1053/j.gastro.2019.01.042

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P0872

CORRELATION OF BILE ACID FRACTIONS AND LIVER STRUCTURAL CHANGES IN CHILDREN WITH NON-ALCOHOLIC STEATOHEPATITIS

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Introduction: Changes in the liver structure in children with non-alcoholic steatohepatitis (NASH) may be accompanied by liver fibrosis progression as a result of both cholestasis and metabolic complications.

Aims & Methods: To determine the relationship of liver structural changes with bile acids fractions of bile and carbohydrate metabolism features.

Methods. 37 children with nonalcoholic steatohepatitis (NASH) were included in prospective cohort study. An average age of patients was ($12,15 \pm 2,51$) years. The presence of liver fibrosis and steatosis was carried out with transient elastometry (FibroScan®502Touch, Echosens, France) and controlled attenuation parameter (CAP) measurement. The presence of NASH was determined according to gender-specific alanine-aminotransferase levels. Liver structure with sonography (Ultrasign, Soneus P7, Ukraine) was investigated. Bile acids in bile were evaluated by thin layer chromatography. Serum insulin content was determined by ELISA test kit (DRG International Inc, Germany). Homeostatic model assessment (HOMA) for insulin resistance (IR) was used with HOMA-IR index calculation.

Results: The correlation analysis revealed the presence of a direct positive association between the taurocholic acid fraction in the gallbladder’s bile with sonographic parameters such as the left liver lobe size ($r = 0,487$,

$p < 0.05$), taurodeoxycholic acid fraction - with the portal vein diameter ($r = 0.458$, $p < 0.05$). In hepatic bile portion a direct positive correlation between taurodeoxycholic acid fraction ($r = 0.547$, $p < 0.05$), glycocholic acid fraction ($r = 0.547$, $p < 0.05$), glycodeoxycholic acid fraction ($r = 0.511$, $p < 0.05$) and portal vein diameter was established. Insulin and HOMA-IR levels correlated positively with glycocholic acid fraction of hepatic bile ($r = 0.667$, $p < 0.05$ and $r = 0.695$, $p < 0.05$, respectively). A direct correlation between gallbladder volume, insulin ($r = 0.24$; $p < 0.05$) and glucose levels ($r = 0.26$; $p < 0.05$) was found.

A strong direct correlation of liver stiffness with cholic acid, bilirubin, cholesterol fractions in gallbladder's bile, insulin, HOMA-IR levels was found. Strong inverse correlation of liver stiffness with taurodeoxycholic acid fraction in hepatic bile was established.

Conclusion: Revealed association of liver structure, bile acids content, carbohydrate metabolism features demonstrated the possibility to influence the liver fibrosis progression by bile acids ratio regulation.

Disclosure: Nothing to disclose

P0873

FIBROSIS PREDICTIVE SCORE IN PATIENTS WITH METABOLIC SYNDROME

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Introduction: The prevalence of the metabolic syndrome (MetS) has increased in Western and developing countries. Patients with MetS have in many cases liver steatosis (NAFLD) and some of them could develop liver fibrosis.

Aims & Methods: The aim of the present study was to develop a simple score that could rule out the presence of significant fibrosis and could be used in daily practice in patients with MetS in order to identify more easily patients at risk.

204 patients with metabolic syndrome (MetS) were prospectively enrolled. Evaluation of liver fibrosis was made using Transient Elastography (FibroScan), performed in fasting conditions, with M and XL probes. Reliable liver stiffness measurements (LSM) were defined as the median value of 10 LSM with an IQR/median $< 30\%$. Subjects characteristics, epidemiological data and biochemical tests were recorded. Every patient was evaluated by ultrasound (US) for identification of the presence of steatosis. Steatosis severity was graded using a semi-quantitative scale (S0-no steatosis; S1-mild steatosis; S2-moderate steatosis; S3-severe steatosis). For developing a score for stratifying the risk of at least significant fibrosis, we used univariate and multivariate regression analysis. The Receiver Operating Characteristic (ROC) curve was employed to illustrate the diagnostic ability. The cut-off value for significant fibrosis was > 8.2 kPa [1].

Results: Out of 204 patients with MetS reliable LSM were obtained in 179 patients (87.7%). The mean age was 62.5 ± 10.8 years, 50.2% were males and the mean BMI was 32.2 ± 5.64 kg/m². At least significant fibrosis (F ≥ 2) was found in 22.9% (41/179) patients. To formulate the fibrosis predicting score, all clinical variables associated with at least significant fibrosis, with $p < 0.05$ in the univariate analysis were considered in a multivariate regression model (BMI, female gender, presence or absence of steatosis

evaluated by US and HDLc). According to the power of correlation, by consensus, we attributed 1 point for BMI > 31.4 kg/m², 1 point for female gender, 1 point for S1 at ultrasound, 1.5 point for S2 at US, 2 points for S3 and 1 point for HDLc < 47 mg/dL. By adding the number of points for each parameter we obtained a predictive score with an AUROC of 0.698; 95%CI[0.606;0.790]. At an optimal cut-off value < 3.5 , our score could be used to rule-out the risk for developing at least significant fibrosis (NPV 89.2%), with acceptable Se (75%) and Sp (63.8%).

Conclusion: A simple score consisting of body mass index (BMI), gender, HDLc, severity of steatosis evaluated by ultrasound can exclude the MetS patients at risk of having at least significant fibrosis in clinical practice.

References: 1. Eddowes P, Sasso M, Allison M et al. Accuracy of FibroScan Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. *Gastroenterology*. 2019;156(6):1717-1730. doi:10.1053/j.gastro.2019.01.042

Disclosure: Ruxandra Mare received speaker fee from Terapia, and travel grant from Philips Ioan Sporea received speaker fee and travel grants from Philips, Siemens, General Electric, Abbvie, Zentiva. Alina Popescu received speaker fee and travel grants from Philips, General Electric, Abbvie, Zentiva, Astra Zeneca. Sirli Roxana received speaker fee and travel grants from Philips, Abbvie, Zentiva

P0874

SERUM DEACYLATED GHRELIN CORRELATES NEGATIVELY WITH LIVER STEATOSIS

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Introduction: Ghrelin is an adipokine that plays an important role in metabolic syndrome. Until recently deacylated ghrelin was considered an inactive ghrelin form and most of studies only addressed acylated ghrelin. Recent studies show that deacylated ghrelin could act protective and diminish the negative impact of acylated ghrelin in the metabolic process. Liver steatosis is a condition tied to metabolic syndrome, and nonalcoholic liver disease is considered as a hepatic manifestation of metabolic syndrome. In this study we wanted to assess the correlation of acyl and deacylated ghrelin serum levels with the severity of liver steatosis.

Aims & Methods: In this study we prospectively included 71 male and female patients initially admitted for polypectomy of colonic polyps. In all patients we determined serum values of acylated, deacylated ghrelin and insulin, as well as presence of metabolic syndrome defined by International Diabetes Federation (IDF) definition. Liver steatosis was determined by ultrasound of the liver, defined by a Hamaguchi score more than 2, and severe steatosis by a score more than 4.

Results: According to IDF definition 46 of 71 patients (64.8%) had MS, 80.2% had a Hamaguchi score > 2 and 43.6% a Hamaguchi score > 4 what was classified as severe steatosis. We found that glucose, insulin and HOMA-IR values correlated negatively with the value of deacylated ghrelin ($p = 0.049$, $p = 0.001$ and $p = 0.001$ respectively). There was no statistically significant correlation of glucose, insulin and HOMA-IR with the levels of acylated ghrelin or acylated to deacylated ghrelin ratio. We also found no statistically significant correlation of presence of MS defined by IDF with the concentrations of acylated and deacylated ghrelin or their ratio. However,

we found a statistically significant negative correlation of deacylated ghrelin levels and the severity of liver steatosis defined by Hamaguchi score ($p = 0.01$), while levels of acylated ghrelin and the acylated to deacylated ghrelin ratio showed no statistical significance ($p > 0.05$).

Conclusion: Deacylated ghrelin is an important adipokine in the regulation of metabolic process. Patients with lower levels of deacylated ghrelin had a higher steatosis grade according to Hamaguchi score, as well as a less favorable metabolic profile, what was not observed for acylated ghrelin.

Disclosure: Nothing to disclose

P0875

PREDICTIVE FACTORS FOR ADVANCED FIBROSIS IN PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Non alcoholic fatty liver disease (NAFLD) has dramatically increased in concert with the epidemics of both obesity and type 2 diabetes, being a major cause of liver-related morbidity and mortality worldwide. In recent years, several non-invasive panels have been performed to identify patients with steatosis or advanced fibrosis. Transient elastography (Fibroscan) is the most available and validated non invasive tool used in clinical practice to assess fibrosis in NAFLD patients.

Aims: The aim of this study was to determine the predictive factors for advanced fibrosis evaluated by Fibroscan in patients with NAFLD

Methods: A prospective descriptive study conducted in the department of hepato-gastroenterology of our university hospital, including patients with NAFLD diagnosed by abdominal ultrasound and referred to our unit for a regular monitoring and a specialized management. Clinical and anthropometric parameters including waist circumference, arterial hypertension and type 2 diabetes were assessed. Biological parameters were: AST, ALT, GGT, ALP, HDL cholesterol, triglycerides, fasting glucose. We used Fibroscan to assess fibrosis in fasting patients for at least 2 hours. Correlation was analyzed by Spearman's correlation test. $P < 0.05$ was considered as statistically significant.

Results: A total of 87 patients were included. The mean age was 49.4 years [15-81] with a female predominance of 79.3%. The mean of body mass index was 32.6 kg / m² (20-55 kg / m²). The mean of waist circumference was 104.5 cm (67-138 cm). A history of type 2 diabetes was found in 37.9%, arterial hypertension in 34.5% and dyslipidemia in 41.4%. The mean of: GGT level was 61,84 u/l, ALP was 93 u/l, ALAT level was 35,2 u/l, AST level was 27,8 u/l, Triglycerides level was 1.55 g/l, HDL cholesterol level was 0,48 g/l and fasting glucose level was 1,28 g/l. The mean Fibroscan value was 5,8Kpa. 79,4% had a median value < 7.1 Kpa [F0-F1], 17,1% had a median value < 7.1 and $< 12,5$ Kpa [F2-F3] and 3,4% had a median value ≥ 12.5 Kpa (Advanced fibrosis). In bivariate analysis, predictive factors of advanced fibrosis were : waist circumference ($P = 0.004$), GGT level ($P = 0.001$), AST level ($P < 0,0001$), ALT level ($P < 0,0001$), Triglycerides level ($P = 0.02$) and fasting glucose level ($P = 0.03$). However, after multivariate analysis regression only AST level ($P < 0,001$), ALT level ($P < 0,003$), triglycerides level ($P < 0.004$) were significant predictors of advanced fibrosis.

Conclusion: The results of this study suggest that AST level, ALT level, triglycerides level are independent predictors of advanced fibrosis evaluated by Fibroscan in NAFLD patients. Advanced fibrosis and complications should be regarded as the outcomes to be prevented when patients with metabolic syndrome or liver tests disorders are managed.

Disclosure: Nothing to disclose

P0876

WHAT IS THE PERFORMANCE OF FIB4 SCORE FOR NON-INVASIVE EVALUATION OF FIBROSIS IN NON ALCOHOLIC FATTY LIVER DISEASE?

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is currently the most frequent form of chronic liver disease, being a major cause of liver-related morbidity and mortality worldwide. In recent years, several non-invasive panels have been performed to identify patients with steatosis or advanced fibrosis. Considering non-invasive biomarkers, FIB-4 is an easy score suggested by studies to be used in clinical practice, while transient elastography (Fibroscan) is the most useful imaging tool to assess the fibrosis stage in NAFLD patients.

Aims & Methods: The aim of this study was to determine the performance of FIB4 score compared to Fibroscan for evaluation of fibrosis in patients with NAFLD.

A prospective descriptive study conducted in the department of hepatogastroenterology of our university hospital, including patients with NAFLD diagnosed by abdominal ultrasound and referred to our unit for a regular monitoring and a specialized management. We used two non-invasive methods to assess fibrosis: "Fibroscan" in fasting patients for at least 2 hours and FIB4 score calculated by an online application on the website: www.mdcalc.com using 4 parameters: Age, AST, ALT, Platelet count. Spearman's test was used to correlate bivariate analysis. Results were considered significant if P was less than 0.05.

Results: A total of 87 patients were included. The mean age was 49.4 years [15-81] with a female predominance of 79.3%. The mean of body mass index was 32.6 kg / m² (20-55 kg / m²). The mean of waist circumference was 104.5 cm (67-138 cm). A history of type 2 diabetes was found in 37.9%, arterial hypertension in 34.5% and dyslipidemia in 41.4%. The mean Fibroscan value was 5,8Kpa. 79,4% of patients had a median value < 7.1 Kpa [F0-F1], 17,1% had a median value < 7.1 and $< 12,5$ Kpa [F2-F3], and 3,4% had a median value ≥ 12.5 Kpa [F4]. The mean of FIB4 score was 1,04. 79,2% had a score $< 1,45$ (negative predictive value of 90% for advanced fibrosis), 17% had a score $< 1,45$ and $< 3,25$ and 3,7% had a score $\geq 3,25$ (positive predictive value of 65% for advanced fibrosis). Bivariate analysis found a significant correlation of fibrosis stage evaluated by Fibroscan and FIB4 score ($P < 0.0001$), with a correlation coefficient $r = 0,71$.

Conclusion: Our results found a significant correlation between FIB4 score and Fibroscan. That suggests that FIB4 score could be a wise tool in combination with others biomarkers to assess fibrosis if Fibroscan is not available.

Disclosure: Nothing to disclose

P0877

QUANTIFICATION OF LIVER STEATOSIS USING TWO DIFFERENT ULTRASOUND-BASED METHODS IN COMPARISON WITH CAP

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Introduction: AttPLUS and SSpPLUS, two methods implemented on the new AixplorerMACH®30 ultrasound system (Supersonic Imagine, Aix-en-Provence, France), allow the simultaneous quantification of ultrasound attenuation in the liver and of the intrahepatic speed of sound.

Aims & Methods: The aim of this study was to evaluate the ability of Att PLUS & SSp PLUS to detect, quantify and grade hepatic steatosis (HS) using Controlled Attenuation Parameter (CAP) (FibroScan, EchoSens) as the reference method.

We prospectively enrolled 147 consecutive subjects with or without different chronic hepatopathies in whom HS was evaluated in the same session by means of 3 ultrasound-based techniques: CAP (FibroScan, EchoSens), Att PLUS and SSp PLUS (Aixplorer MACH® 30 system, Supersonic Imaging) in fasting conditions. We defined reliable HS measurements for CAP as the median value of 10 measurements with an interquartile range/median (IQR/M) < 30%, and for Att Plus and SSp Plus, as the median value of 5 measurements with an IQR/M < 30%, following the recommendations of the manufacturer, performed in the right liver lobe, in an area without vessels or artifacts during neutral respiratory apnea. To discriminate between steatosis stages by CAP we used the following cut-off values: S1 (mild) - 274 dB/m, S2 (moderate) - 290 dB/m, S3 (severe) - 302 dB/m. [1] Correlation analysis was used to determine the relationship between HS values obtained using the 3 techniques.

Results: Reliable HS measurements were obtained in 144/147 (97.9%) subjects by Att PLUS & SSp PLUS and in 141/147 (95.9%) by CAP. In the final analysis we included 140 subjects, with reliable HS measurements, aged 54.5±13.1 years. Based on the cut-off values proposed (CAP) steatosis distribution was S0- 65/106 (46.4%); S1-8/140 (5.7%); S2- 10/140 (7.1%); S3- 62/140 (44.2%). A medium positive correlation was found between Att Plus and CAP, ($r=0.4$, $p<0.0001$). Instead, a strong positive correlation was found between SSp Plus and CAP values ($r=0.72$, $p<0.0001$). The mean SSp values decreased with increasing of steatosis grade and were the following for each group: S0:1526±24.4 m/s, S1:1517±30 m/s, S2:1513±29 m/s, and S3:1508±26.5 m/s. The best SSp cut-off value for predicting moderate/severe steatosis (S3) using CAP as the reference method was: SSp mean ≤ 1515 m/s (AUC 0.89, Se=68.42%, Sp=93.9%, PPV=88.4%, NPV=80.2%).

Conclusion: In our study, of the steatosis quantification techniques implemented on the new Aixplorer MACH® 30 system, we found only SSp Plus to correlate with CAP and could be used in the detection, quantification and grading of liver steatosis.

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Disclosure: Nothing to disclose

P0878

A NEW APPROACH TO THE DIFFERENTIAL DIAGNOSIS OF FATTY LIVER DISEASE: ACUTE ETHANOL EXPOSURE ON ERYTHROCYTES IN VITRO

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Introduction: The fatty liver disease (FLD) includes the alcoholic (AFLD) and non-alcoholic (NAFLD) genesis of the disease. The first one is associated with the use of ethanol by patients in hepatotoxic doses, the second one is mainly associated with metabolic syndrome. Despite the coincidence of the most of metabolic pathways of AFLD and NAFLD, the course, prognosis, and disease treatment approaches shall be different, which determines the importance of the differential diagnosis of FLD, especially at the early stages of its development.

Aims & Methods: The purpose of this research is to study the differences in viscoelastic parameters of erythrocytes (deformation amplitude, summarized viscosity, rigidity) in an interaction dynamics with ethanol *in vitro* for patients with non-alcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease (AFLD), to use its results in the differential diagnosis.

Materials and methods. 50 males have been examined, among them: 24 with NAFLD (46.5±1.5 y.o.), 24 with AFLD (48.6±1.2 y.o.), the degree of liver fibrosis in all patients corresponded to F0-1 (Fibroscan FS-502, ECHOSENS). The study of viscoelastic parameters of the erythrocytes has been performed by the method of dielectrophoresis using an electro-optical cell detection system. In the experiment plotted against time, the levels of the erythrocytes' indicators before and after the *in vitro* exposure for 300 s of 10 µl of 0.02% ethanol solution have been estimated.

Results: As for the patients with NAFLD after exposure to ethanol, a reduction in the deformation amplitude of the erythrocytes has been determined, associated with increased summarized indicators of viscosity and rigidity; and on the contrary, as for the patients with AFLD, an increase in the ability to deformation of the erythrocytes with a reduction in the summarized viscosity and rigidity ($p<0.01-0.05$) have been ascertained. Direct correlations of the etiology of FLD with summarized viscosity ($r=0.592$, $p<0.0001$) and rigidity ($r=0.567$, $p<0.0001$) and the reverse association with the amplitude of cell deformation ($r=-0.551$, $p<0.001$) were revealed reflecting more pronounced shifts in the parameters in the alcoholic genesis of FLD. The different dynamics of the viscoelastic parameters of erythrocytes is probably due to the adaptation of red blood cells to chronic alcoholization during AFLD (with structural and functional changes) and the absence of such in patients with NAFLD. An inverse reaction of the cells to ethanol exposure has made it possible to distinguish between patients with fatty liver disease of different genesis with sensitivity of 87.5%, specificity of 96.2%, prognostic value of positive result equal to 95.4% and of negative result equal to 89.3%, as well as an accuracy index of 92%.

Conclusion: The proposed method for distinguishing fatty liver disease of various genesis is promising due to its simplicity, high throughput, high diagnostic accuracy and low costs.

Disclosure: Nothing to disclose

P0879

TREATMENT OF ALCOHOL USE DISORDER IN PATIENTS WITH ALCOHOLIC HEPATITIS

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Introduction: Alcoholic hepatitis (AH) is associated with high short-term mortality (Osna et al., 2017). The only treatment of proven benefit for AH is abstinence (Verill et al., 2009). It is well known that patients who continue to use alcohol in the setting of AH have higher rates of hepatic decompensation and death (Potts et al., 2013). Historically, few patients have received treatment for alcohol use disorder (AUD) and there has been little integration of addictions services into the care of patients with AH (SAMHSA, 2014).

While alcohol relapse prevention medications have been studied in the general population, research on their efficacy and safety in patients with liver disease has been limited, leading to variable approaches to pharmacotherapy in practice.

Aims & Methods: In patients admitted to hospital with AH, we sought to determine the frequency at which AUD was identified as a problem, non-pharmacologic therapies were prescribed, and the prescribing patterns of relapse prevention medications. A retrospective chart review was conducted of all patients admitted with AH to the Health Sciences Centre in Halifax, Nova Scotia, Canada, from April 2015 to July 2019.

The clinical diagnosis of AH was confirmed per consensus definition; cases were included if meeting probable or definite criteria (Crabb et al., 2016). Patient alcohol use was documented and reported as grams of alcohol per day. Patient Model for End-Stage Liver Disease (MELD) score and Maddrey's Discriminant Function (MDF) were recorded. To rule out other confounding factors to patient presentation, relevant history regarding prescription drug, cocaine and intravenous drug use, imaging for portal or hepatic vein thrombosis, and serology for alpha-1 antitrypsin, Wilson disease, autoimmune hepatitis and viral hepatitis were recorded.

Charts were reviewed to determine if AUD was identified as a problem during admission, if patients were referred to psychosocial interventions, and whether alcohol relapse prevention medications were prescribed at discharge and up to one year after discharge.

To evaluate outcomes, 30-day readmission rates and mortality at 365 days were recorded.

Basic and descriptive statistical analyses were completed using Stata®.

Results: Thirty-six individuals were admitted with AH during the study period, composed of 52.78% males (n=19) and a mean age of 50.3 years (St dev=11.46 years, range 30 to 75). Participants consumed an average of 196.24 g of alcohol per day (St dev=188.33, range 28 to 728). Mean MELD score was 27 (St dev=15.43, range 14 to 110.2) and mean MDF score was 43.89 (St dev=25.04, range -0.3 to 103).

AUD was listed as a diagnosis in 61% of patients (n=22), and less than half were referred to psychosocial interventions (n=13, 37%). A quarter of patients were prescribed relapse prevention medication at discharge (n=9, 25%). Baclofen was prescribed in 7 out of 9 of the admissions (78%), while naltrexone and gabapentin were each prescribed once (11% each). At one month follow up, five individuals were readmitted to hospital (14.29%). At one year follow up, four deaths were recorded (11.43%). One out of the four patients (25%) who died at one year follow up were prescribed relapse prevention medications, while none were referred to psychosocial interventions.

Conclusion: In patients admitted with AH, AUD is underreported and psychosocial interventions and relapse prevention medications are underutilized in patients who may benefit the most from such interventions.

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Disclosure: Nothing to disclose

P0880

ADAMTS13 DEFICIENCY AND PLATELET ACCUMULATION IN PYRROLIZIDINE ALKALOIDS-INDUCED HEPATIC SINUSOIDAL OBSTRUCTION SYNDROME

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Introduction: Pyrrolizidine alkaloids (PAs) widely exist in plants and can cause liver injury, particular as hepatic sinusoidal obstruction syndrome (HSOS). PAs-HSOS is histopathologically diagnosed with dilatation of sinusoidal space and congestion, collagen deposition and hepatocyte necrosis around the central vein (zone 3). Recently, platelet aggregation in space of Disse was confirmed in mice administered with monocrotaline (MCT), a kind of PA in retronecine-type. A disintegrin-like and metalloproteinase with thrombospondin type 1 motifs-13 (ADAMTS13) plays a pivotal role in regulating platelet accumulation through cleaves von Willebrand factor (vWF) multimers, and the imbalance between ADAMTS13 and vWF would affect hematologic conditions in various hepatic diseases, but their functions haven't been reported in PAs-HSOS yet.

Aims & Methods: We first hypothesized that ADAMTS13 deficiency contributed to platelet accumulation in PAs-HSOS. Our team previously established the PAs-HSOS mouse model using Tusanqi, a commonly misused herb containing PAs in China. By adopting the PAs-HSOS induction by Tusanqi in mice, liver tissue of mice in controlled and Tusanqi-HSOS group were applied to RNA-Sequencing to find the possible gene that would participate in the pathogenesis of PAs-HSOS.

Furthermore, to be more accurate, we treated C57BL/6 mice with MCT, a purified PA, at the concentration of 400mg/kg, and sacrificed them after 144h MCT challenge. Mice liver function tests and blood routine tests were applied. Hepatocyte necrosis, CD31 and ICAM-1 was measured by immunohistochemistry. Platelet accumulation, vWF deposition and fibrinogen was measured by immunofluorescence. We also applied electron microscopy to directly detect platelet accumulation in mice liver. Hepatic ADAMTS13 level was measured by qPCR, Western blot and immunofluorescence.

Results: RNA-sequencing results of Tusanqi-HSOS group have shown that platelet activation pathway was significantly down regulated compared to the controlled group (P=0.0015), and complement and coagulation cascade was also down regulated (P<0.0001). Also, *Adamts13* expression

was decreased dramatically in Tusanqi-HSOS group ($P=0.0035$). Then, in the MCT-induced PAs-HSOS mouse model, after 144 h MCT challenge, serum concentrations of aspartate aminotransferase ($P=0.0324$) and alanine aminotransferase ($P=0.0284$) were significantly higher than the controlled group, while mouse platelet account was lower ($P=0.0072$). Such changes could largely represent the liver injury in PAs-HSOS mouse model. Meanwhile, the liver tissue in PAs-HSOS group was positive for CD41 compared to the controlled group in the immunofluorescent assay, and electron microscopy findings directly showed platelet accumulation in the Disse space. Hepatic ADAMTS13 level was found decreased in both western blot and immunofluorescent assay in PAs-HSOS group. Serum ADAMTS13 level was also decreased in PAs-HSOS group. As ADAMTS13 cleaves vWF multimers into smaller forms, we also found that vWF deposition was increased in PAs-HSOS mouse liver tissue both in western blot and immunofluorescence assay. Meanwhile, mouse serum vWF levels were elevated.

Conclusion: This finding first reported platelet activation and coagulation pathway is down regulated in PAs-induced HSOS mice model through RNA-Sequencing. Our results also suggested the link between ADAMTS13 deficiency, hepatic platelet accumulation and PAs-HSOS, which indicates that targeting ADAMTS13 might provide a novel therapeutic approach to PAs-HSOS.

Disclosure: Nothing to disclose

P0881

MANAGEMENT OF N-ACETYL CYSTEINE COMPLICATIONS AND DEVELOPMENT OF TREATMENT ALGORITHM

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Introduction: In the UK, Paracetamol (PCM) is one of the most common agents of intentional self-harm¹. In England and Wales, there were 219 deaths from poisoning by paracetamol and its compounds in 2016². For patients qualifying for treatment, N-acetylcysteine (NAC) is drug of choice³. Intravenous (IV) NAC is associated with anaphylactoid reactions, most of which are mild and easily treated. Life-threatening reactions appear to be uncommon. In UK, TOXBASE is available to hospitals for further advice about the management of patients presenting with paracetamol overdose (OD). However, it can be sometimes overwhelming and time consuming when looking for specific information in acute settings. Due to recent emergence of Paracetamol overdose, we decided to do a quality improvement project (QIP) for service improvement and patient safety.

Aims & Methods: 2 PDSA (Plan-Do-Study-Act) cycles were carried out. 1st cycle involved retrospective 6 months audit of patients receiving NAC for PCM OD, in Accident and Emergency (A & E) and Acute Medical Unit. Adverse effects and their management were noted. Questionnaire based survey was done in acute medical team about awareness of complications and subsequent treatment.

Based on results, interventions were done, which included; generation of simple and accessible algorithm (Figure 1, based on TOXBASE) to manage common complications; algorithm posters placement in various departments; small group teachings and awareness sessions during handover in acute take. 2nd cycle involved prospective 4 months audit. Adverse event and resultant management noted.

Results: 60 patients in 1st cycle received NAC infusion. 8.3% (5/60) patients developed adverse reaction. 2 had nausea and vomiting and 3 developed rash. 1 of these 5 had previous anaphylactic reaction to NAC in past. Management was heterogenous and in 2 cases it led to early discontinuation of

NAC. Survey showed 86% (95/110) of doctors not aware of adequate management plans. In 2nd cycle there were 36 patients who received NAC, 3 developed adverse reaction, all of them allergic and managed adequately. No early discontinuation of NAC reported.

Conclusion: NAC is generally well tolerated and safe. Knowledge of complications and their effective management enhance the patient safety. Though composite information is provided on TOXBASE but it can be very tedious in bustling settings of A & E and Acute medical take. We recommend use of this simple algorithm to improve care in patients receiving NAC and boost competent management of patients with Paracetamol overdose.

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Disclosure: Nothing to disclose

P0882

SAFETY, EFFICACY AND COST-EFFECTIVENESS OF GLASGOW MODIFIED ALCOHOL WITHDRAWAL SCALE AND SYMPTOM-TRIGGERED DOSING REGIMEN FOR THE MANAGEMENT OF ACUTE ALCOHOL WITHDRAWAL SYNDROME IN AINTREE UNIVERSITY TEACHING HOSPITAL

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Introduction: National Institute for Health and Care Excellence (NICE) estimate that 40% of patients admitted with an alcohol related problem would develop acute alcohol withdrawal syndrome [1]. NICE recommend the use of symptom-triggered dosing regimen rather than fixed dose regimen in managing alcohol withdrawal. The Glasgow Modified Alcohol Withdrawal Scale (GMAWS) is a validated assessment tool that has been acknowledged as easier to use in practice to the Clinical Institute of Withdrawal Alcohol revision scale (CIWA-Ar) as it is less cumbersome [2,3,4]. GMAWS tool was introduced into our local guidance in November 2018.

In this study we demonstrate the effectiveness of managing alcohol withdrawal through the symptom-triggered dosing regimen and the application of GMAWS tool in assessing the severity of alcohol withdrawal.

Aims & Methods: A short survey was conducted across the region at the beginning that determined only 18% of hospitals uses GMAWS tool. A retrospective study was then designed to evaluate the introduction GMAWS and symptoms-triggered dosing regimen in our trust through assessing the length of stay in hospital and number of patients developed delirium tremens (DT).

Results: 419 patients (female 30%, male 70%) were admitted with alcohol withdrawal (January - June 2019). The average age of patients included in the study was 48.8. 29% had a background history of mental health illness and 16% had a previous diagnosis of DT. Interestingly only 8% developed DT during the study period.

We also found that 42% of the patients had one night hospital stay and 36% stayed between 2-5 nights. The average day the patients needed to complete detox was found to be 2.32 days and the total dosage of Chlordiazepoxide used by all patients during their stay was 262.6mg.

Conclusion: Our study has shown that usage of GMAWS and symptoms-triggered dosing regimen in managing alcohol withdrawal are safe, efficient and cost-effective.

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Disclosure: Nothing to disclose

P0883

DAY-4 LILLE SCORE IN EARLY PREDICTION OF CORTICOSTEROID RESPONSE FOR PATIENTS WITH SEVERE ACUTE ALCOHOLIC HEPATITIS

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Introduction: Corticosteroids are indicated for patients with severe acute alcoholic hepatitis (SAH), defined by a Maddrey`s discriminat function (MDF) score >32 [1]. Lille score helps to discriminate the steroid responders (< 0.45) and non-responders (>0.45) after 7 days of treatment [2]. The aim of this study is to evaluate whether using Lille score at day 4 (LM4) is as useful as Lille at day 7 (LM7), in order to determine response to therapy earlier.

Aims & Methods: A retrospective study was performed during October 2015-February 2020 in a tertiary Department of Gastroenterology and Hepatology. All consecutive patients with SAH, without contraindications to corticosteroids were enrolled. All patients received 40 mg of Prednisone per day and response was assessed with LM4 and LM7, according to the cut-off value (CUV< 0.45 responder and CUV>0.45 non responder). 28-day mortality was assessed between LM4 and LM7 responders and nonresponders.

Results: 72/101 patients (71.3%) with SAH had MDF>32 out of which 52/101 (51.5%) received corticosteroids (83.1% male, mean age 54±9.38 years). The median value MDF was 57±30. The mean value for LM4 was 0.64±0.29, vs 0.58±0.32 for LM7, p=0.43. There was no difference between the proportion of patients with a responder LM4 versus LM7, 15/52 (29%) vs 20/52 (38.5%), p=0.33. The area under the ROC curve for predicting mortality for LM 4 was similar to LM 7 (0.67 vs. 0.68, respectively, p=0.9). By using LM4 and LM7 with CUV>0.45, the 28-day mortality was higher in nonresponder (27% and 31%) than in responder cohort (20% and 15%). If we take LM4 with CUV< 0.45 into consideration, 90.3% of patients were correctly identified as compared with LM7.

Conclusion: LM4 could be used instead of LM7 in predicting the response to corticosteroids in SAH, as well as 28-day mortality. Using LM4 we could avoid a prolonged use of this therapy with its complications.

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Disclosure: Nothing to disclose

P0884

THE IMPLEMENTATION OF A PATHWAY FOR MANAGING ALCOHOL RELATED BRAIN INJURY IN ACUTE CARE SETTINGS

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Introduction: Alcohol related brain injury (ArBI) is a term used to cover the neuropsychiatric conditions that occur as a result of prolonged alcohol misuse. Throughout the years there was lack in identifying and managing these patients by clinicians, which resulted in prolonged hospital admissions and/or high re-admission rates to hospital. Identifying these patients early in the acute setting through capacity and cognitive assessment will ensure the appropriate care for them and facilitate the appropriate and safe discharge plans. Following a local clinical audit looking at the number of patients admitted with a background history of alcohol excess and cognitive impairment, we have implemented a one-page pathway for responsible clinicians to follow if a diagnosis of ArBI was suspected. We think that this simple pathway is one of the first pathways that summarises the management plan for patients with suspected ArBI.

Aims & Methods: We identified the patients who had cognitive impairment on the background of alcohol excess over a 10 month period. Patients with dementia, stroke or being on end of life pathway have been excluded. We looked at how the cognitive impairment was assessed and whether the Montreal Cognitive Assessment Tool was used. We also looked at the length of hospital stay and re-admission rates for those who were not diagnosed with ArBI.

Results: 4.3% (47) of patients with alcohol misuse were identified as having cognitive impairment during their hospital stay over a period of 10 months (January-October 2018). Mostly were male (72%) with a median age of 53.3. Only 8 had a MOCA done during their hospital stay. 23% (11) were diagnosed with ArBI where (17%) 8 were confirmed by psychiatric team. All of the patients with cognitive impairment had brain imaging that excluded intracranial pathology. The over all average length of stay in hospital was 7 days (shortest stay 1 day and longest stay 73 days). 2 patients who never had MOCA done had at least 4 admissions within 6 month period with similar presentation.

Conclusion: Our data show the importance of using MOCA in confirming level of cognitive impairment in patients with alcohol misuse in order to identify the ones with ArBI early and arrange the appropriate discharge and follow up. As a result we have implemented a simple one-page pathway for clinicians to follow if ArBI is suspected. The pathway advises on the appropriate investigations and pharmacological treatment and when to involve the psychiatric team. We think the usage of this pathway will improve the care of such patients and reduce hospital stay and re-admission rates.

Disclosure: Nothing to disclose

P0885

CONGLOMERATED ASSOCIATION OF LIGHT DRINKING TYPE AND DURATION ON THE DEVELOPMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE: A NATIONWIDE POPULATION-BASED LONG TERM FOLLOW UP STUDY

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Introduction: High dose alcohol ingestion is well-known risk factor for alcoholic liver disease. However, there have been conflicting results on effect of light drinking on development of non-alcohol fatty liver disease (NAFLD).

Aims & Methods:

Aims: We aimed to evaluate the effect of low dose of alcohol ingestion on the development of NAFLD using nationally representative long term follow up study.

Methods: We used data from the Korean health examinee (HEXA) study which was conducted during 2004-2013 at baseline, and 2012-2017 at first follow up period. After exclusion of participants with above moderate dose of alcohol ingestion (>20 g of alcohol /day for men and women), and without data on fatty liver index (FLI), we finally analyzed the data of 132523 of participants (aged ≥40 years). Accordance to alcohol ingestion duration for 'current drinker' and alcohol withdrawal duration for 'ex-drinker', we divided participants into 'current-light drinker (≤10 year of alcohol ingestion)', 'current-light drinker (>10 year of alcohol ingestion)', 'ex-light drinker (≤10 year of alcohol withdrawal)', 'ex-light drinker (>10 year of alcohol withdrawal)', and life time alcohol abstainer group. The NAFLD risks were compared among groups in univariate and multivariate analysis.

Results: At baseline study, 5399 cases (10.06%) from light drinker group and 4623 cases (5.86%) from life time abstainer group had NAFLD ($p<0.001$). When participants divided into life time abstainer, ex-light drinker (<10 year of duration), ex-light drinker (≥10 year of duration), current light drinker (<10 year of duration), and current light drinker (≥10 year of duration), NAFLD cases were 4623/78829(5.86%), 164/1099(14.92%), 408/3197(12.8%), 513(4.87%), and 3986(11.39%) were reported, respectively. After adjusting for age, sex, diet pattern, smoking, regular exercise, diabetes mellitus, hypertension, and socioeconomic status, the odds ratio for each group with reference group as life time abstainer was 1.27[0.89-1.81] ($p=0.19$), 1.49[1.02-2.24] ($p=0.04$), 1.16[1.00-1.35] ($p=0.06$), and 1.69[1.35-2.10] ($p<0.001$), respectively.

Conclusion: Even light drinking, more than 10 year of ingestion duration could be the independent risk factor to the risk of NAFLD while more than 10 years of alcohol withdrawal was relatively similar risk as with that of life time abstainer. Physicians should keep in mind that light drinking duration and withdrawal time are independently associated with the risk of NAFLD.

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Disclosure: Nothing to disclose

P0886

A NOVEL ROLE OF THE P53 FAMILY IN BACTERIA-HOST-INTERACTION - ANALYZING THE PATHOMECHANISM OF SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: Spontaneous bacterial peritonitis (SBP) - a life-threatening complication of liver cirrhosis - is driven by bacterial translocation. Although it is known that bacterial translocation is promoted by immune dysfunctions, increased intestinal permeability and bacterial overgrowth in patients with liver cirrhosis, the detailed mechanism of SBP development is still unknown. With wide-ranging function in immunity and cellular stress response, involvement of the p53 family in liver cirrhosis and SBP is conceivable. Therefore, we studied the regulation of p53 family members and their target function in an *in vitro* model and intestinal biopsies of patients with liver cirrhosis.

Aims & Methods: Intestinal biopsies of 19 controls and 9 patient with liver cirrhosis (5x child-pugh A, 4x child-pugh C) were included in the study. For analysis of the p53 family, mRNA and protein levels of p53 and p73 were analyzed. Moreover, we established an intestinal *in vitro* model with HCT-116 epithelial cell line. To mimic bacterial overgrowth, HCT-116 cells were cocultured with *Escherichia coli* (*E. coli*) at different concentrations for up to 4 hours. Regulation of p53 and p73 were studied via qPCR and Western blot. Additionally, p53 family target functions were analyzed *via* cell death induction upon bacterial stimulation.

Results: No significant differences with regard to age or sex were observed between liver cirrhosis and control patients. Two child-pugh class C patients developed SBP after colonoscopy while another two child-pugh class C patients had exhibited a SBP prior to colonoscopy. Compared to controls, patients with advanced liver cirrhosis showed diminished p53 and p73 on RNA and protein level. In accordance, cocubation of HCT-116 cells with *E. coli* resulted in a decrease of p53 and p73 protein levels in a time- and dose-dependent manner. Despite reduced levels of p53 family members, a high rate of cell death after *E. coli* stimulation was shown.

Conclusion: Advanced liver cirrhosis is accompanied with reduction in intestinal expression of p53 family members. Active bacteria trigger these reduction and this mechanism might contribute to prolonged bacterial replication and SBP development. To antagonize a high bacterial burden, intestinal epithelial cells induce cell death. In summary, there is a new role of p53 regulation in bacterial infection like SBP

Disclosure: Nothing to disclose

P0887

UNRAVELING THE PATHOMECHANISM OF SBP - BACTERIAL TRANSLOCATION IS TRIGGERED BY MUCUS REDUCTION AND A DESTABILIZED EPITHELIAL BARRIER

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Introduction: Spontaneous bacterial peritonitis (SBP) is one of the most harmful complications of liver cirrhosis. Despite antibiotic therapy, SBP reoccurs in 70 % and worsens chances of survival. Therefore, SBP remains a serious problem and new treatment options are challenging. Up to now, the detailed pathomechanism of SBP is unknown. Bacterial translocation (BT), especially of commensal *Escherichia coli* (*E. coli*) drives SBP. Risk factors of BT are dysbiosis, a suppressed immune system and a destabilized intestinal epithelial barrier. To unravel underlying pathomechanisms of SBP, regulation of the epithelial barrier including mucus and cell junctions was analyzed.

Aims & Methods: Intestinal biopsies of 19 controls and nine patients with liver cirrhosis were included. To study mucus thickness, frozen sections of intestinal biopsies were stained with alcian blue. E-cadherin and occludin were analyzed on protein level via immunohistochemistry. Caco-2 cells were treated with *E. coli* bacteria that were isolated from ascitic fluid of two patients with SBP. As control, heat-inactivated bacteria were used. Caco-2 cells were stimulated with *E. coli* bacteria directly or separated by a semipermeable membrane. Mucin regulation (*MUC-2* and *MUC5AC*) and cell junctions (E-cadherin and occludin) were analyzed on RNA and protein level.

Results: With 13.7 +/- 4.6 µm mucus, patients with liver cirrhosis displayed decreased mucus thickness compared to controls with 16.1 +/- 6.2 µm. Mucosa of patients with SBP showed broken occludin rings and faded staining. Additionally, a loss of structure and a weaker staining of E-cadherin was observed. Bacterial stimulation with viable but not heat-inactivated *E. coli* resulted in a decrease of E-cadherin and occludin and a reduced mucin production of Caco-2 cells. A direct interaction of *E. coli* with epithelial cells promoted downregulation of cell junction components, especially E-cadherin.

Conclusion: Increased epithelial permeability requires a direct interaction of bacteria with intestinal epithelial cells. Therefore *E.coli* trigger mucus reduction. The diminished mucus layer in liver cirrhosis patients facilitates a direct interaction, promoting a destabilized epithelial barrier and driving BT and SBP.

Disclosure: Nothing to disclose

P0888

RIFAXIMIN SOLUBLE SOLID DISPERSION TABLETS MODIFY GUT MICROBIAL FUNCTION, AS SHOWN BY INCREASED FAECAL SECONDARY BILE ACID LEVELS COMPARED WITH PLACEBO, IN PATIENTS WITH EARLY DECOMPENSATED CIRRHOSIS

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Introduction: The gut microbiota plays an important role in regulating bile acid homeostasis, and microbial dysbiosis can impact the overall concentration and the composition of the bile acid pool (eg, lower ratio of secondary to primary bile acids). Secondary bile acid profiles have been postulated as a potential marker for cirrhosis progression. Modulating gut microbiota dysbiosis using a nonsystemic antibiotic such as rifaximin may beneficially impact the bile acid pool.

Aims & Methods: This post hoc subanalysis evaluated faecal bile acid profiles in patients with early decompensated cirrhosis treated with rifaximin soluble solid dispersion (SSD) tablets, an investigational rifaximin formulation with improved water solubility, while maintaining minimal systemic exposure. In a phase 2, randomised, double-blind, placebo-controlled, dose-finding trial, adults with cirrhosis and ascites (grade ≥1), with no history of oesophageal variceal bleeding or spontaneous bacterial peritonitis, received rifaximin SSD or placebo once nightly for 24 weeks (ClinicalTrials.gov identifier: NCT01904409). This post hoc subanalysis evaluated data from patients receiving rifaximin SSD immediate-release (IR) tablets 40 mg (most efficacious dose) or placebo once nightly at bedtime. Stool samples were collected at screening (Day -21 to Day -7), after 24 weeks of treatment, and at 2 weeks post-treatment (Week 26). Bile acids were extracted from stool, and profiles were determined using high-performance liquid chromatography, per published methods (Kakiyama G, et al. *J Lipid Res.* 2014;55[5]:978-990).

Results: Stool samples were analysed for 48 patients in the rifaximin SSD IR 40-mg group and 50 patients in the placebo group. At screening, mean (SD) total faecal bile acid concentrations were 12.2 (18.6) and 8.2 (9.8) µmol/g of stool for rifaximin SSD IR 40 mg and placebo, respectively; 3.8 (10.8) and 1.6 (3.2) µmol/g of stool for primary bile acids; and 7.7 (10.2) and 5.7 (8.4) µmol/g of stool for secondary bile acids. A higher mean concentration of total and secondary bile acids was observed in the rifaximin SSD IR 40-mg group versus placebo at Weeks 24 and 26; at Week 26 for total bile acids, the difference was 0.6 µmol/g (95% CI, 0.1-1.1; *P*=0.02), and for secondary bile acids, 0.9 µmol/g (95% CI, 0.0-1.7; *P*=0.02).

Conclusion: Rifaximin SSD IR 40 mg once nightly for 24 weeks increased the total and secondary faecal bile acid concentrations versus placebo in patients with early decompensated cirrhosis. This indicates that rifaximin SSD IR treatment has an impact on gut microbial function. Larger trials are warranted to explore rifaximin SSD IR and the role of faecal bile acid profiles as a marker for disease progression and complications of cirrhosis.

References: N/A

Disclosure: Supported by Salix Pharmaceuticals. GK, WMP, HZ, LRT, and DZ report no conflicts of interest. ZH is an employee of Salix Pharmaceuticals. JSB reports being a consultant for Salix Pharmaceuticals.

P0889

A MURINE MODEL OF HEPATIC ENCEPHALOPATHY: VALIDATION AND NEUROBEHAVIORAL TESTING

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Introduction: Hepatic encephalopathy (HE) is a severe complication of chronic liver disease (CLD). According to the ISHEN guidelines, an experimental model of HE resulting from decompensated liver cirrhosis (Type C HE) exhibits a.o. the following features: 1) CLD with portal-systemic shunting, 2) a range of symptoms varying from minimal HE to coma and 3) hyperammonemia¹. Common bile duct ligation (BDL) has been considered as a valid model for HE in rats. Although improved mouse models are needed to facilitate studies of molecular genetics of HE, no HE mouse model has been comprehensively validated yet.

Aims & Methods: This study aims to evaluate whether BDL induction in mice can reproduce the clinical and biochemical characteristics of type C HE.

7-week-old, male Swiss mice underwent either BDL (n=14) or sham control (n=13). 10-week-old, male C57Bl/6 mice underwent either BDL (n=15) or sham control (n=13). After 6 (Swiss) or 8 (C57Bl/6) weeks, mice were sacrificed and liver damage/liver synthetic function was assessed through plasma liver tests (AST, ALT, bilirubin) and blood albumin levels. Liver fibrosis was assessed histologically through Sirius Red staining. Spleen to body weight ratio was measured as an indicator of portal hypertension. Plasma ammonia levels were analysed.

Both at baseline and at 6 (Swiss) or 8 (C57Bl/6) weeks after induction, general locomotor activity (spontaneous activity in a glass cylinder, open field test), motor coordination (difficult beam traversal), anxiety (open field test) and spatial memory (Y-maze) were assessed.

Results: Both in Swiss and C57Bl/6 experiments, liver enzymes (AST (p<0.0001), ALT (p<0.0001)) and bilirubin (p<0.0001) were elevated. However, only C57Bl/6 mice had decreased albumin levels (p<0.0001) when compared to their respective sham controls. In both strains, mice developed significant fibrosis/cirrhosis at the chosen endpoint. Spleen to body weight ratio was significantly elevated in BDL mice of both strains (p<0.0001). Importantly, only C57Bl/6 mice had elevated plasma ammonia concentrations vs. sham controls (p<0.0001).

Decreased rearing behavior (C57Bl/6: p<0.0001; Swiss: p=0.0055) and decreased travelling distance in the open field (C57Bl/6: p<0.0001; Swiss p=0.0295) was observed in BDL mice of both strains when compared to sham controls. Motor coordination was only impaired in C57Bl/6 BDL mice as evidenced by increased beam traversal time (+64%, p=0.0007). Additionally, only C57Bl/6 BDL mice exhibited more anxiety-like behavior in the open field (p<0.0001) than sham controls. Finally, spatial memory in the Y-maze was not significantly different between groups in both strains. Importantly, all C57Bl/6 BDL mice exhibited a constant neuro-phenotype and elevated ammonia concentrations, suggesting adequate reproducibility of this model.

Conclusion: We demonstrate that BDL in C57Bl/6 mice is a valid and reproducible murine HE model. Behavioral testing showed increased motor incoordination and anxiety, as well as motor inactivity. Spatial memory was however not affected.

Despite similar levels of histological liver damage, Swiss mice did not exhibit the biochemical characteristics of HE. They did however have decreased levels of spontaneous activity, though milder than in C57Bl/6

mice. This suggests a sickness behavior rather than a real manifestation of HE. Therefore, beam traversal and anxiety testing seem more reliable assessors of the HE phenotype.

References: 1. Butterworth, R.F., et al. Experimental models of hepatic encephalopathy: ISHEN guidelines. *Liver International*, 2009 Jul;29(6):783-8.

Disclosure: Wouter Claeys: Wouter Claeys is sponsored by the Research Foundation Flanders (11A6420N). Hans Van Vlierberghe: Hans Van Vlierberghe is senior clinical investigator of the Research Foundation Flanders. All other authors have declared no conflicts of interest.

P0890

VARICEAL RECURRENCE 4 YEARS BEYOND ENDOSCOPIC BAND LIGATION IN HEPATITIS C PATIENTS WHO ACHIEVED SUSTAINED VIROLOGICAL RESPONSE POST DIRECT ACTING ANTIVIRAL THERAPIES

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Introduction: Direct antiviral therapies (DAAs) are highly effective and safe altering the disease prognosis and burden. Sustained virologic response (SVR) is achieved nowadays in > 90 percent of the patients and is related to improvements in liver function, fibrosis and overall survival. Furthermore, Portal hypertension is expected to be improved with virological response, parallel to improvements in hepatic inflammation and liver fibrosis.

Aims & Methods: **Aim:** to evaluate the rate of recurrence of esophageal varices by long duration follow up in patients treated with different regimens of DAAs and achieved SVR.

Methods: 176 patients were infected with chronic HCV, achieved 24 weeks SVR post DAAs treatment, and had history of endoscopic obliteration of their esophageal varices and continuing on maximum tolerable dose of propranolol. They were subjected to follow up upper gastrointestinal endoscopy repeated every 6 months until four years.

Results: 52 patients (29.5%) had recurrence of esophageal varices during the 4-year follow up upper GIT endoscopy. By multivariate analysis, the platelet count was the only variable with significant association, P-Value=0.007*. By ROC we identified baseline platelet count of 96,000/ micro liter as having 100 % sensitivity (95 % confidence interval- CI [91%- 100%]) and 74% specificity (95% CI [65%- 81%]).The positive predictive value was 62 % (CI [51%-72%]) and the negative predictive value was 100% (CI [95%-100%]).The area under the curve (AUC) = 0.84.

Conclusion: Patients who achieved SVR post DAAs shows significant decrease in the recurrence of esophageal varices post endoscopic obliteration. Baseline platelet count is strongly predictor for the recurrence.

Disclosure: Nothing to disclose

P0891 WITHDRAWN

P0892

TIMING OF PARACENTESIS AND OUTCOMES IN HOSPITALIZED PATIENTS WITH DECOMPENSATED CIRRHOSIS

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Introduction: Ascites is the most common complication of cirrhosis and a common reason of admission in hospital, placing significant burden on the healthcare system. Timing of paracentesis is important in the outcomes in hospitalized patients.

Aims & Methods: Aim of the study was to assess the outcomes of patients with cirrhosis who underwent paracentesis within the 12 h following admission compared to patients who underwent paracentesis later than 12h. The present study included 307 patients with cirrhosis and ascites admitted to our hospital. Demographic data and laboratory tests were recorded. Time to paracentesis since admission was assessed and early paracentesis (EP) was defined as < 12 h from admission and delayed paracentesis (DP) as > 12 h from admission. Patients were assigned to the EP group and DP group. Length of hospital stay (LOS), occurrence of spontaneous bacterial peritonitis (SBP), in-hospital mortality rate and readmission rate were assessed in each group.

Results: Out of 307 patients with cirrhosis and ascites, 185 (60.2%) patients underwent paracentesis: EP was performed in 65 (35.1%) patients and DP in 120 (64.9%) patients. There was a significant shorter LOS in the EP group vs. DP group (6.7 days vs. 12.2 days, $p < 0.05$). There was no association between timing of paracentesis and diagnosis of SBP ($p < 0.05$). Patients in the EP group had lower in-hospital mortality rate than those with DP: 6.5% vs. 17.5%, $p=0.04$. Regarding one-year readmission rate of the patients with documented timing of paracentesis, 76 (24.7%) patients were at least once readmitted with continuous hospitalization: 20 (26.3%) were in the EP group and 56 (73.7%) were in the DP group ($p < 0.05$).

Conclusion: EP (within 12 h following admission) decreases LOS, in-hospital mortality, readmission rate and can decrease also healthcare utilization.

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P0893 WITHDRAWN

P0894

ACUTE-ON-CHRONIC LIVER FAILURE IS INDEPENDENTLY ASSOCIATED WITH HIGHER MORTALITY IN PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: Spontaneous bacterial peritonitis (SBP) accounts for 24% of infections in cirrhotic patients with ascites. Although therapy has greatly improved, the prognosis of SBP carries an in-hospital mortality around 20% to 40%. Ascites defines cirrhosis as decompensated. When SBP takes place, it worsen prognosis greatly. ACLF has been welcomed as the definition of an additional step between DC and death, which is characterized by multi-organ failure.

Aims & Methods: The purpose of this study is to analyze if EASL-CLIF definition of ACLF is able to predict mortality in cirrhotic patients with SBP. This is a historical cohort study conducted in a public tertiary care teaching hospital. Data from medical records from January 2009 to July 2016 were obtained by searching the hospital electronic database for samples of ascites collected in the period. Electronic and physical medical records were hand-analyzed and patients were included if they were over 18-years old, with cirrhosis and an ascites fluid compatible with spontaneous bacterial peritonitis. It was included 69 patients. ACLF was defined using EASL-CLIF criteria, derived from CANONIC study. Liver-specific scores were calculated and Kaplan-Meier survival analysis was used for univariate analysis and a stepwise approach to the Cox regression for multivariate analysis.

Results: All-cause mortality was 44%, 56.5% and 74% for 28-, 90- and 365-day, respectively. The prevalence of ACLF was 58%. Of these, 65% grade 1, 17.5% grade 2 and 17.5% grade 3. All cause-mortality was, respectively, 27.6%, 41.4% and 55.2% for 28-, 90- and 365-day for DC, 57.7%, 61.5% and 76.9% for 28-, 90- and 365-day for ACLF grade 1, 57.1%, 57.1% and 71.4% for 28-, 90- and 365-day for ACLF grade 2 and 100% for 28-, 90- and 365-day for ACLF grade 3.

Variable	28-day survival (hazard ratio - 95% CI)	90-day survival (hazard ratio - 95% CI)
PPI Use	3.5 (1.4-8.4) $p = 0.005$	2.5 (1.2-5.1) $p = 0.01$
ALT (< 40 U/L)	3.8 (1.5-9.4) $p = 0.004$	2.4 (1.1-5.1) $p = 0.01$
Hemoglobin (> 9 g/dL)	12.5 (3.6-42.8) $p < 0.001$	4.2 (1.7-10.8) $p = 0.002$
Higher albumin (g/L) - per unit	-	0.56 (0.34-0.91) $p = 0.01$
Inactive Alcoholism	3.1 (1.2-7.9) $p = 0.01$	-
ACLF absent	20.2 (3.9-103.2) $p < 0.001$	6.1 (1.8-20.1) $p = 0.003$
Liver-specific scores		
Lower MELD - per unit	0.84 (0.75-0.93) $p = 0.002$	0.9 (0.83-0.97) $p = 0.05$
Lower CLIF-SOFA - per unit	1.1 (1.04-1.3) $p = 0.01$	1.1 (1.01-1.26) $p = 0.05$

[Model for multivariate analysis for survival]

Kaplan-Meier univariate analysis was performed. ACLF absent, male sex, use of PPI (proton-pump inhibitor), furosemide and NSBB (non-selective beta-blockers), inactive alcoholism, total bilirubin lower than 4 mg/dL, INR (International Normalized Ratio) lower than 1.3, AST and ALT lower than 40 U/L, hemoglobin higher than 9 mg/dL, creatinine lower than 2 mg/dL, serum levels of albumin and lower MELD, CLIF-SOFA and CTP

scores were associated with higher 28-day and 90-day survival, using as statistically significant a p value below 0.2 for inclusion in multivariate analysis.

Cox regression, using the stepwise approach, was reduced until every variable had a level of independent significance of $p < 0.05$. Use of PPI, ALT lower than 40 U/L, Hemoglobin higher than 9, active alcoholism, absence of ACLF and lower values of MELD and CLIF-SOFA scores were independently associated with higher 28-day survival. Use of PPI, ALT lower than 40 U/L, hemoglobin higher than 9, higher levels of albumin in the serum, absence of ACLF and lower values of MELD and CLIF-SOFA scores were independently associated with higher 90-day survival.

Conclusion: The presence of ACLF and higher CLIF-SOFA scores were independently associated with higher 28- and 90-day mortality in cirrhotic patients admitted due to SBP.

Disclosure: Nothing to disclose

P0895

PREVALENCE OF OESOPHAGEAL VARICES AND PREDICTORS OF BLEEDING IN PATIENTS WITH CHRONIC LIVER DISEASE IN A NIGERIAN POPULATION

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Introduction: Variceal haemorrhage is one of the most devastating consequences of portal hypertension. It is an ominous event associated with a 15% to 20% 6 week mortality for each episode with a 1 year mortality of 40% inspite of endoscopic and pharmacologic therapies.

The risk of bleeding from oesophagogastric varices is 25-35% for both alcoholic and nonalcoholic cirrhosis with the majority of initial bleeding episodes occurring within the first year from the time of diagnosis.

The high mortality associated with each bleeding episode makes it a necessary to predict as well as prevent the first bleed. It is therefore important to see if there are parameters that can non-invasively predict variceal bleeding as endoscopy is not readily accessible in LMICs.

Aims & Methods: This study sought to determine the prevalence of oesophageal varices and the predictors of variceal bleeding in patients with chronic liver disease in a Nigerian population.

This was a descriptive cross sectional study, in which 102 patients with chronic liver disease were recruited consecutively to participate in the study. Blood sample for liver function tests, serum urea and creatinine, platelet count, prothrombin time/INR was taken from each patient, and an ultrasound scan of the abdomen as well as an upper gastrointestinal tract endoscopy was carried out on each patient to determine the presence or absence of oesophageal varices as well as presence or absence of evidence of variceal bleeding. A proforma was used to document the socio-demographic characteristics, clinical features as well as results of laboratory/radiologic parameters.

Non-invasive predictors of variceal bleeding were determined. Test of association between categorical variables was carried out using the Chi-Square Test. Test of association between abnormally distributed continuous variables was carried out using the Mann-Whitney U test. Logistic regression analysis was used to detect predictors of bleeding. The sensitivity and specificity of some non-invasive predictors were determined by the area under curve (AUC) at various cut off levels using the receiver operating characteristic (ROC) curve analysis. Statistical significance was set at P value < 0.05.

Results: A total of 102 subjects, M: F 4:1 with a mean (SD) age of 47.2(±10.1)

years completed the study. Seventy (68.6%) were hepatitis B surface antigen positive. The prevalence of varices in the studied population was 77.5%. Thirty-three (32.4%) of the recruited subjects bled from ruptured varices.

On multivariate analysis, large varices ($p=0.010$, OR 2.222; 1.680-2.940) and red colour sign ($P=0.027$, OR 6.878; 1.379-20.599) were predictors of oesophageal variceal bleeding on endoscopy while older age ($P=0.002$, OR 1.118; 1.041-1.202), advanced Child Pugh class ($P< 0.001$, OR 0.009; 0.002-0.052) and low platelet count ($P=0.029$, OR 0.935; 0.880-0.993) were non-invasive predictors of oesophageal variceal bleeding. Platelet count had moderate diagnostic accuracy with sensitivity of 79% and specificity of 81%, AUC=0.825.

Conclusion: Platelet count, a simple, cheap and available investigation, can be used as a non-invasive predictor of variceal bleeding. In resource poor settings like Nigeria with limited endoscopy services, the platelet count can be used to select those patients who will benefit from prophylactic therapy to prevent variceal bleeding.

Disclosure: Nothing to disclose

P0896

RISK FACTORS OF PORTAL VEIN THROMBOSIS IN CIRRHOTIC PATIENTS

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Introduction: Portal vein thrombosis (PVT) is a significant and common event during cirrhosis, worsening portal hypertension and impacting survival after transplantation. The use of nonselective beta-blockers (NSBBs) for prevention of variceal bleeding has been hypothesized being responsible of increasing the development of PVT as it reduces portal vein inflow velocity. However, it is still debated and risk factors are not completely known.

Aims & Methods: The aim of our study was to assess risk factors and clinical features of PVT in cirrhotic patients. We performed a retrospective study in which we included cirrhotic patients admitted in our department over 5 year's period. Diagnostic of cirrhosis was based on histology or clinical, laboratory and imaging findings. The diagnosis of PVT was made by ultrasound performed every 6 months. The presence of PVT was evaluated with logistic regression analysis where the independent variables were those significant ($p < 0.005$) in the univariate analysis.

Results: Overall, eighty-four patients were included with a mean age of 54.58 ± 14.25 years. Viral hepatitis was the most frequent etiology of cirrhosis. Child-Pugh score A was prevalent (50.6%). PVT was diagnosed in 16 patients (19%). Thrombosis was partial in most cases (62.5%) and portal cavernoma occurred in 12.5 % of patients with PVT. We didn't find a significant difference between PVT group and non-PVT group regarding using NSBBs therapy ($p=0.097$) nor with grade of varices or MELD score. PVT was significantly associated with large splenomegaly > 16 cm ($p=0.001$), Child-Pugh score ($p=0.028$), hypoalbuminemia ($p=0.003$), platelet to spleen diameter ratio ($p= 0.038$) and platelet-albumin-bilirubin (PALBI) score ($p= 0.01$). In logistic regression analysis, only longitudinal diameter of the spleen > 16 cm was an independent factor associated with PVT [HR 5.31; 95% CI: 1.344-21.051; $p=0.017$].

Conclusion: In our study, NSBBs therapy was not significantly correlated with a higher risk of portal vein thrombosis. However large splenomegaly was an independent factor associated with the development of portal thrombosis.

Disclosure: Nothing to disclose

P0897 WITHDRAWN

P0898

EFFICACY AND SAFETY OF INTRAVENOUS ALBUMIN FOR NON-SPONTANEOUS BACTERIAL PERITONITIS INFECTION AMONG PATIENTS WITH CIRRHOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Bacterial infection is a common cause of acute-on-chronic liver failure (ACLF) and death among cirrhosis. The benefit of intravenous (IV) albumin among cirrhosis with non-SBP infection remains unclear as individual studies are underpowered to detect the survival benefit of IV albumin.

Aims & Methods: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to evaluate the efficacy and safety of intravenous albumin for non-SBP infection among cirrhosis patients. We performed a systematic search of electronic databases (Pubmed, MEDLINE and Clinicalkey) up to 1st December 2019. Studies evaluating IV albumin for non-SBP infection were selected. Using random effect model, the pooled odds ratio (OR), 95% confidence interval (95%CI) and heterogeneity were assessed.

Results: A total of 3 RCTs (406 subjects) fulfilling the inclusion criteria among 218 citations were identified. There was no significant heterogeneity across included studies. In this meta-analysis, we found that the pooled risk of renal impairment (RI) (OR=0.58, 95%CI: 0.28-1.23, $P=0\%$), mortality at 30 days (OR=1.61, 95%CI: 0.87-3.00, $P=0\%$) as well as mortality at 90 days (OR=1.30, 95%CI: 0.81-2.07, $P=0\%$) were similar between albumin and control group.

Pooled event of pulmonary edema occurred more commonly in albumin group (OR 5.17, 95%CI 1.62-16.47, $P=0\%$). More subjects achieved resolution of ACLF in IV albumin group as compared to control group (OR=0.11, 95%CI: 0.02-0.69, $p=0.02$).

Conclusion: Albumin did not reduce the risk of RI and mortality, yet increased the risk of pulmonary edema. Albumin may promote recovery of ACLF, however, more data is required to validate this benefit.

Disclosure: Nothing to disclose

P0899

HEPATIC OSTEODYSTROPHY IN CIRRHOSIS DUE TO ALCOHOL-RELATED LIVER DISEASE

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Introduction: Hepatic osteodystrophy, including osteoporosis, is an abnormal bone metabolism related with chronic liver diseases. Osteoporosis is associated with an increased risk of bone fractures, with a significant

impact on morbidity, mortality and healthcare costs. Nevertheless, bone disorders tend to be undervalued in cirrhosis due to alcohol-related liver disease (ALD cirrhosis).

Aims & Methods: We aimed to assess the prevalence of hepatic osteodystrophy and osteoporosis in ALD cirrhosis. We conducted a prospective observational study including patients with ALD cirrhosis between September/2017-December/2018. Bone mineral density was determined by dual energy X-ray absorptiometry at the lumbar spine and the femoral neck. Hepatic osteodystrophy was defined as a T-score below -1 SD and osteoporosis as a T-score below -2,5 SD.

Results: 94 patients included. 24,5% (n=23) had prior fragility fractures and 10 patients suffer new osteoporotic fractures during the study period. Hepatic osteodystrophy was diagnosed in 79,8% (n=75) and osteoporosis in 21,3% (n=20) of cases. Femoral neck was more severely affected. Patients with hepatic osteodystrophy presented significantly lower weight and body mass index ($p<0,001$) and significantly worse Child-Turcotte-Pugh ($p<0,001$) and MELD-Na scores ($p<0,01$). Patients with osteoporosis had also lower weight and body mass index ($p<0,01$). Female patients and those with prior fragility fractures were more likely to suffer from osteoporosis ($p<0,05$).

Conclusion: Our study revealed a high prevalence of hepatic osteodystrophy and osteoporosis in patients with ALD cirrhosis and a concerning high rate of fragility fractures. Bone mineral density should be assessed in order to allow early diagnosis and implementation of preventive measures.

Disclosure: Nothing to disclose

P0900

INFECTIONS AND MULTIDRUG-RESISTANT ORGANISMS IN PATIENTS WITH DECOMPENSATED LIVER CIRRHOSIS ADMITTED TO AN INTENSIVE-CARE UNIT

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Introduction: Infections are a common complication in patients with liver cirrhosis and are associated with a greater risk of organ-dysfunction and short-term mortality^{1,2}.

Aims & Methods: The aim of our study was to determine the most common infections in patients with liver cirrhosis admitted to an Intensive-Care Unit (ICU), namely the ones associated with multidrug-resistant organisms (MDROs). We analyzed their association with ICU and hospital length-of-stay and in-hospital mortality.

We conducted an observational retrospective study on patients with an established histologic or clinical diagnosis of hepatic cirrhosis admitted to a tertiary hospital's ICU from 2016 until 2019. Sociodemographic, clinical and laboratory data were collected from computer records. Statistical analysis was performed using Stata[®] 15 and a p-value < 0.05 was considered statistically significant.

Results: We included 58 patients, 81% men, with a mean age of 57±10 years. Alcohol abuse was the main cause of liver cirrhosis (86%), followed by hepatitis C infection (19%). Main causes of admission were variceal bleeding (n=18), infections (n=11) and grade 2-3 acute-on-chronic liver failure (ACLF) (n=13). On admission, the patients had a mean Model for

End-Stage Liver Disease - Sodium score of 26 ± 10 points and Chronic Liver Failure - Sequential Organ Failure Assessment score of 11 ± 2 points, with ACLF in 80% (n=46) of the cases.

In our population, 44 patients had at least one infection diagnosed during hospital stay, with the isolation of one or more microbiological agents in 77% (n=34) of these patients. We identified Gram-negative bacteria, Gram-positive bacteria and fungi in 67%, 50% and 20% of the cases, respectively. From these agents, 38% were MDROs (n=13), the most frequent being extended spectrum beta-lactamase (n=7) and *Klebsiella Pneumoniae* carbapenemase (n=5) producing bacteria.

The most common infections were the following: spontaneous bacterial peritonitis (43%), pneumonia (41%), bacteremia (39%) and urinary tract infection (18%); more than half of the infections were nosocomial (63%). In 38% and 71% of the patients with infections there was recent antibiotic use in the past three months and previous hospital admission due to cirrhosis decompensation, respectively. However, no statistically significant association between these risk factors and infections by MDROs was found (p=0.546).

Infections by MDROs were associated with a higher incidence of sepsis and septic shock in these patients (p=0.022 and p=0.038, respectively), but no difference between groups was found regarding hospital mortality (p=0.378), which was 59% in our study population. Infected patients had longer ICU admissions than uninfected ones (p=0.008), and this difference was even more significant for patients with MDROs, with a length of stay in an ICU of 16 ± 10 days contrasting with 8 ± 5 days (p< 0.001). Patients with MDROs also had longer general hospital stays (46 ± 37 days versus 23 ± 20 days) (p=0.005).

Conclusion: The incidence of MDROs infections has been increasing overall, namely in healthcare units. In our study we found a high prevalence of MDROs infections in patients with decompensated liver cirrhosis admitted to an ICU, which is associated with a longer length-of-stay, stressing the importance of systematic screening for early diagnosis of severe infection. The most common type of infections and microbiology were similar to those identified in other international studies. This underlines the importance of preventing the emerging problem of antimicrobial resistance and its disease burden.

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Disclosure: Nothing to disclose

P0901

APPLICATION OF THE NEW CLIF-CACLF SCORE IN MORTALITY PREDICTION

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Introduction: Acute over chronic hepatic failure (ACLF) is defined as acute hepatic decompensation associated with at least one organ failure of extrahepatic origin. ACLF is associated with a poor prognosis. To predict mortality during this syndrome, a new prognostic score CLIF C ACLF (Chronic Liver Failure Consortium - Acute-on-Chronic Liver Failure) has been developed and validated.

Aims & Methods: The aim of our study is to apply this score in our patients and compare its performance with other prognostic scores.

This is a retrospective study of cirrhotic patients hospitalized for edema-toascitic decompensation over a period of 5 years. We excluded patients with hepatocellular carcinoma. The diagnosis and grading of ACLF was defined according to CANONIC study criteria. The CLIF C ACLF score is calculated by combining the CLIF OF (chronic liver failure organ failure score) diagnostic score with the patient's age and white blood cell count according to the following formula: $CLIF-C\ ACLF = 10 \times (0.33 \times CLIF-OF + 0.04 \times Age + 0.63 \times \ln(GB) - 2)$. The CLIF OF is determined by adding up the individual organ failures.

Results: Seventy-six inpatients were included, with a sex ratio (M/W= 0.9). The mean age was 60.9 years. The etiologies of cirrhosis were: hepatitis C (30.2%), hepatitis B (14.4%), non-alcoholic steatopathy (15.7%), alcoholic (9.2%) and various etiologies (36.8%). Cirrhosis had been evolving on average for 27 months. Twenty-one patients developed ACLF. Grade 1 was the most frequent (47.6%) followed by grade 2 (33.3%) and then grade 3 (23.8%). For patients with ACLF, the mean MELD score was 28 and cirrhosis was classified as Child C in 80% of cases. The high CLIF C ACLF score with a threshold set at 43 corresponding to a sensitivity of 91% and a specificity of 69% was a predictor of mortality within 28 days (p< 0.001), as was the Meld score (p=0.01) and the Child (p=0.012) but to a lesser degree. The area under the curve was 0.995 for the CLIF C ACLF versus 0.88 for the Meld score and 0.82 for the Child score. A CLIF C ACLF score > 50 was associated with mortality in 100% of cases.

Conclusion: In our study, the new CLIF C ACLF score is the most efficient in predicting short-term mortality (within 28 days). Current studies tend to define an upper limit of this score corresponding to 100% mortality and therefore to limit therapeutic efforts.

Disclosure: Nothing to disclose

P0902

EVOLUTION AND CLINICAL IMPACT OF CARDIAC VARICES AFTER ENDOSCOPIC BAND LIGATION

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Introduction: Gastric varices are less prevalent than esophageal varices in patient with portal hypertension, but their presence can have an impact over outcomes and mortality. According to their location, they are classified as gastroesophageal varices including cardiac varices (CV) and isolated gastric varices. Previous studies have shown conflicting results regarding the impact of endoscopic variceal ligation (EVL) on the natural history of CV.

Aims & Methods: We aimed through this study to investigate changes in CV and their clinical impact in patients treated with EVL. We conducted a retrospective study over 5 years (2012-2017) including patients presenting portal hypertension treated with EVL for primary or secondary prophylaxis of variceal bleeding. Patients with previous gastric varices bleeding receiving endoscopic therapy and those with hepatocellular carcinoma were excluded. Endoscopic data at first EVL and during follow-up, laboratory investigations and outcomes were collected.

Results: Overall, 89 patients were included: 45 men and 55 women. The mean age was 55.93 ± 14.17 years. The main cause of portal hypertension was cirrhosis (94.3%). EVL was performed mainly for secondary prophylaxis. Cardiac varices were observed in 23 patients (26%) at first presentation. After EVL treatment, eradication was achieved in 88.8% of patients and variceal recurrence after first eradication occurred in 41% of patients.

We noticed that that patients with CV needed significantly more number of rubber bands used to achieve eradication than patients with esophageal varices only (mean $19,70 \pm 9,30$ versus $15,74 \pm 7,20$ respectively, $p=0.033$). However, CV were not correlated with the size of the esophageal varices, the spleen size, platelet count, number of EBL sessions or duration until eradication. After eradication, CV disappeared in almost half of patients (45%). The persistence of cardiac varices after EVL treatment was significantly associated with variceal recurrence after eradication in univariate analysis ($p=0.029$).

Conclusion: In our study, cardiac varices were significantly associated to higher number of rubber bands used and the persistent varices after eradication were significantly correlated to variceal recurrence.

Disclosure: Nothing to disclose

P0903

CUMULATIVE INCIDENCE AND SHORT-TERM MORTALITY OF ACUTE-ON-CHRONIC LIVER FAILURE

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Introduction: Acute-on-chronic liver failure (ACLF) is a recently recognized syndrome characterized by acute decompensation of liver disease, organ failure and high short-term mortality. This syndrome may occur at any time of the natural history of the chronic liver disease.

Aims & Methods: Estimate the cumulative incidence of ACLF after a first acute decompensation of cirrhosis and evaluate short-term mortality rate in patients with this syndrome. This retrospective inception cohort included all cirrhotic patients with a first episode of acute decompensation admitted in Gastroenterology ward of the Military Hospital of Tunisia, from January 2010 to December 2018.

Results: Eighty-nine patients were included. The main causes of cirrhosis were viral infection and non-alcoholic fatty liver disease. The mean period of follow-up was 26,94 months. Among the 89 patients, 39 (43,8%) developed ACLF. The cumulative rate of ACLF after a first acute decompensation was 23 and 51% at one and five years, respectively. Patients with alcoholic cirrhosis were more likely to develop this syndrome ($p=0.001$). Bacterial infections were the main cause of ACLF. Almost all patients exhibited signs of systemic inflammation. The prevalence of bacterial infection in ACLF patients was 74,35%. Third-generation cephalosporins were the mostly used as the first-line therapy and penems as escalating treatment. Among patients with ACLF, the 28-day mortality exceeded 50%. The 28-day mortality in ACLF grade 1, 2 and 3 was 37,5, 66,7 and 63,6%, respectively.

Conclusion: ACLF is the most common cause of death in cirrhosis. This syndrome is associated with excessive systemic inflammation and high short-term mortality.

Disclosure: Nothing to disclose

P0904

AGE-PLATELET INDEX A PREDICTOR OF LONG TERM VARICEAL BLEEDING RECURRENCE AFTER ENDOSCOPIC BAND LIGATION

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Introduction: Variceal bleeding marks a turning point in the natural history of portal hypertension. Indeed, despite the efficiency of oesophageal band ligation (EVL), patients experiencing acute bleeding from oesophageal varices remains at high risk of long term variceal bleeding recurrence. However risk factors are not well established.

Aims & Methods: The aim of our study was to assess long-term results of secondary prophylaxis with EVL and to investigate predictors of variceal bleeding recurrence. We enrolled cirrhotic patients treated by EVL after acute oesophageal bleeding over 5 years period. Patients with hepatocellular carcinoma or gastric varices bleeding were excluded. We calculated non-invasive scores: Meld, Meld-Na, Fib-4, APRI, ALBI score and age-platelet index for each patient at the moment of the first EVL. We retrospectively gathered clinical data, endoscopic findings, as well as results of variceal ligation and collected outcomes. All patients were followed until death or until December 2019.

Results: Overall, seventy-nine patients were included: 43 men and 36 women. The mean age at the first EVL was 54.76 years. The main cause of cirrhosis was viral hepatitis C or B in almost half of the cases (51%). At presentation, 38% had Child A, 50.6 % had Child B and 11.4% had Child C. In total 242 EVL sessions were performed. The mean duration of follow up after esophageal variceal eradication was $53.78 \pm 24,7$ months. First eradication was achieved in 84% of cases. Long term variceal bleeding recurrence occurred in 45.5% of patients. Age-platelet index was the only non-invasive score significantly associated with bleeding recurrence. Mean age-platelet index in patients with bleeding recurrence was 8.22 versus 6.81 in patients without recurrence ($p=0.006$). The area under the receiver operating characteristics curve (AUC) of age-platelet index in predicting variceal bleeding recurrence was 0.765 (95% CI: 0.598-0.932, $p=0.009$).

Conclusion: Age-platelet index is a simple and useful tool that may be a good predictor of long term variceal bleeding recurrence as it combines platelet count reflecting portal hypertension and age.

Disclosure: Nothing to disclose

P0905

CAN ACUTE KIDNEY INJURY AND CHRONIC KIDNEY DISEASE INDEPENDENTLY INFLUENCE THE PROGNOSIS OF CIRRHOTIC PATIENTS?

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Introduction: Kidney dysfunction is considered a key factor to determine the prognostic outcome of cirrhotic patients.

Aims & Methods: **Aim:** To assess the impact of acute kidney injury (AKI) and of chronic kidney disease (CKD) in the 6 month-mortality rate of cirrhotic patients.

Methods: Cohort retrospective study, including consecutive hospital admissions of cirrhotic patients meeting the criteria of AKI. We established a minimum follow up time of 6 months. A univariate analysis tested the correlation between the covariables and the outcome variable (6-month-mortality rate). The statistically significant variables were included in multivariate logistic regression models. As a second endpoint, we assessed the correlation between AKI and the development of CKD in three months.

Results: We included 87 patients. Alcohol abuse was the main etiology for cirrhosis in 90.8% of the cases. AKI grade 1 was observed in 74.7% of the patients, from whom 58.5% met criteria for the sub-stage 1a, AKI grade 2 in 13.8% and AKI grade 3 in 11.5%. The 6-month-mortality rate was of 25.3%. An AKI grade > 1a, the maximum value of creatinine and the repetition of episodes meeting criteria for AKI were statistically associated with the development of chronic kidney disease in three months. Only the latter persisted statistically significant in the multivariate model (OR 11.6 [3.05-44.43] $p < 0.001$).

An AKI grade >1a, the repetition of episodes meeting criteria for AKI, a MELD-NA > 20 and previous diagnose of CKD were associated with 6-month mortality. Only the latter persisted statistically significant in the multivariate model (OR 3.58 [1.05-12.12] $p = 0.04$).

Conclusion: The repetition of episodes meeting the criteria for AKI is associated with an 11 time-fold increase of the risk of developing CKD. The development of CKD increases the 6-month mortality rate in almost 3.6 times, a relation not independently verified with the AKI criteria.

Disclosure: Nothing to disclose

P0906

DIAGNOSIS OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION IN PATIENTS WITH COMPENSATED LIVER DISEASE BY TWO-DIMENSIONAL SHEAR WAVE AND TRANSIENT ELASTOGRAPHY OF LIVER AND SPLEEN

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Introduction: Portal hypertension is key prognostic factor in patients with compensated advanced chronic liver disease (cACLD), with major complications starting to occur at the threshold of 10 mmHg as measured invasively by hepatic venous pressure gradient (HVPG), representing clinically significant portal hypertension (CSPH).

Aims & Methods: We aimed to investigate diagnostic performance of two dimensional shear wave elastography by Supersonic imagine (2DSWE-Aixplorer®) and transient elastography (TE-Fibroscan®) to noninvasively diagnose CSPH in patients with cACLD by liver and spleen stiffness measurements (LSM and SSM). Patients with cACLD undergoing HVPG measurements were prospectively included.

cACLD was considered in patients with history of liver disease lasting >6 months, without previous decompensation and either LSM by TE ≥ 10 kPa or presence of morphological features by liver imaging studies suggestive of cACLD. All patients underwent LSM and SSM by TE and 2DSWE in fasting condition, followed by HVPG measurements and transjugular liver biopsy (TJB). Patients with congestive liver, cholestasis, infiltrative liver conditions or ALT > 5x ULN were not included.

Results: We included 76 patients (78.9% males, average age 62 years, 36.8% with alcoholic liver disease, 30.3% with non-alcoholic fatty liver, 14.5% with viral hepatitis B/C). Cirrhosis was histologically confirmed in 67.9% patients, mean HVPG was 10 mmHg, and esophageal varices present in 42.9%.

Correlation between HVPG and LSM by 2DSWE (Pearson $r = 0.82$) or TE ($r = 0.73$) was better as compared to SSM (Pearson $r = 0.655$ for TE and $r = 0.596$ for 2DSWE). Cut-off value of LSM for CSPH by 2DSWE was 20.1 kPa (sens. 80.5%; spec. 94.3%; AUROC 0.926), whereas for TE it was 20.2 kPa (sens. 77.5%; spec. 86.1%; AUROC 0.866). Cut-off value of SSM for CSPH by 2DSWE was 34.8 kPa (sens. 83.3%; spec. 81.5%; AUROC 0.877), and by TE was 43.5 kPa

(sens. 89.3%; spec. 69.7%; AUROC 0.857).

Conclusion: Among patients with cACLD LSM was highly reliable for non-invasive diagnosis of CSPH, better than SSM, and with better diagnostic performance obtained by 2DSWE as compared to TE.

Disclosure: Nothing to disclose

P0907

DETERMINANTS OF OUTCOMES IN AUTOIMMUNE HEPATITIS PRESENTING AS ACUTE ON CHRONIC LIVER FAILURE WITHOUT EXTRAHEPATIC ORGAN DYSFUNCTION UPON TREATMENT WITH STEROIDS

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Introduction: Autoimmune Hepatitis presenting as acute on chronic liver failure (AIH-ACLF) is a novel entity with limited data on clinical course and management. We assessed outcomes in patients of AIH-ACLF with no extrahepatic organ dysfunction/failure when administered steroids.

Aims & Methods: In this retrospective analysis, clinical data, laboratory parameters, liver biopsy indices and prognostic scores like model for end stage liver disease (MELD) and Child Pugh scores (CTP) at baseline were computed for patients with AIH-ACLF and compared across strata of incident infections and transplant-free survival. The primary outcome was 90-day transplant free survival. Biochemical remission was assessed and predictors of end points were identified.

Results: 29 patients of AIH-ACLF were included with median follow-up of 4 months. 90- and 180- days transplant-free survival rate of 55.2 (95% CI: 39.7-76.6)% and 30.2(95% CI: 16.7- 54.6)% respectively were attained on steroids. Three patients (10.3%) underwent liver transplant while 16(55.2%) deaths occurred. Infections developed in 12 patients (41.3%), leading to worsening prognostic scores, new onset organ dysfunction/failure and 11 deaths. 7 out of 10 patients (70%) in transplant free survivor group attained biochemical remission on follow-up. MELD score < 24 (sensitivity:68.4%; specificity:80%) and CTP < 11 (sensitivity:78.9%; specificity 90%) had best predictive value for survival, in addition to decrease in MELD score at 2 weeks (sensitivity:78.9%; specificity:70%).

Conclusion: Patients with AIH-ACLF have morbid disease course despite treatment with steroids. Patients with no extra-hepatic organ failure with good baseline prognostic scores may be administered steroids with close monitoring for change in MELD over 2 weeks.

Disclosure: Nothing to disclose

P0908 WITHDRAWN

P0909

ASSESSMENT OF LONG-TERM PROGNOSIS IN PATIENTS WITH VARICEAL BLEEDING: ROLE OF PALBI SCORE

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Introduction: Variceal bleeding is a severe events during cirrhosis in which survival remains the most important end-point. As therapeutic medical and endoscopic strategies had improved, a reliable scoring system is needed for a better prediction of survival. In clinical practice, various scoring systems are used to estimate prognosis, the most important are the Child-Turcotte-Pugh (CTP) score and the Model for End-Stage Liver Disease (MELD) score. ALBI (albumin-bilirubin score) and PALBI (platelet-albumin-bilirubin score) are new scores validated as prognostic models in hepatocellular carcinoma.

Aims & Methods: The aim of our study was to evaluate ALBI and PALBI scores comparing to CTP and MELD scores in assessing long term mortality in cirrhosis with variceal bleeding complication. A retrospective study was conducted including patients followed for cirrhosis over 5 years. Patients with hepatocellular carcinoma were excluded. CPT, MELD, ALBI and PALBI scores were calculated from data for each patient at the first variceal bleeding. Overall survival and outcomes were determined. The prognostic performance of the different scoring system was assessed through the area under the receiver operating characteristics curve (AUROC).

Results: Eighty-four patients with history of variceal bleeding were included. The mean age was of 54.58 ± 14.25 years with a sex ratio of 1.05. Most common etiology of cirrhosis was hepatitis B or C (51,2%) followed by primary biliary cholangitis (7%) and nonalcoholic steatohepatitis (6%). Cirrhosis was decompensated in 38 patients (45%). At presentation, 50.6% had CTP A, 36.1% had CTP B and 13.4 % had CTP C. All patients were treated with endoscopic band ligation with eradication rate of 88%. Long-term variceal bleeding recurrence occurred in half of patients. Mortality rate at 5 years was 19.1%. AUROCs of MELD, CTP, ALBI and PALBI to predict survival were 0.722 [95%CI: 0.573-0.870], 0.756 [95%CI: 0.619-0.893], 0.758 [95%CI: 0.624-0.892], and 0.762 [95%CI: 0.627-0.897], respectively. PALBI had the best correlation.

Conclusion: In our study PALBI showed a better prognostic performance in predicting long term mortality in cirrhotic patients with history of variceal bleeding. Incorporating platelet count in PALBI score may have improved accuracy in predicting outcomes.

Disclosure: Nothing to disclose

P0910

RESISTANCE TRAINING EFFECTS ON MUSCLE STRENGTH AND MUSCLE MASS IN COMPENSATED CIRRHOTIC PATIENTS: PRELIMINARY RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Introduction: Cirrhosis is a chronic disease that impairs liver function. In this group of patients, sarcopenia is highly prevalent, resulting in impaired muscle function and poor clinical prognosis. Resistance training has been widely used to counteract sarcopenia in older patients; however, its safety and efficacy is yet to be determined in cirrhotic patients.

Aims & Methods: The aim of the present 3-arm randomized controlled trial is to verify the efficacy of resistance training to improve muscle strength, muscle thickness and muscle quality in patients with compensated cirrhosis.

Twenty compensated cirrhotic patients Child-Pugh A or B were recruited to the study. After completion of the baseline assessment, participants were randomly assigned to 3 groups: resistance training group (RET; n = 7), active control group (ACG; n = 6) and control group (CG; n = 7). ACG group undertook a low-intensity stretching and walking program once a week, while the CG group underwent monthly clinical follow-up for 24 weeks for 24 weeks. RET group performed two weekly resistance training sessions, with an average duration of 50 minutes and an interval of 48 hours between sessions. Muscle strength was assessed by an isokinetic dynamometer test, and quadriceps femoris muscle thickness and muscle quality assessed by an ultrasound device. Assessments were performed at baseline, 12 and 24 weeks. Differences at baseline levels were analyzed by one-way analysis of variance (ANOVA), while ANOVA adjusted for the baseline levels (ANCOVA) was used to analyze changes over time between groups.

Outcome	Baseline	Week 12	Week 24	Within-group mean differences		
Isokinetic strength, N.m				0 vs. 12	0 vs. 24	12 vs. 24
RTG	159.7±30.7	171.8±31.8	167.4±24.0	12.1* [1.1, 23.1]	7.7 [-5.9, 21.3]	-4.5 [-14.1, 5.2]
ACG	129.5±51.0	132.1±56.3	133.1±42.4	2.6 [-5.6, 10.9]	3.6 [-12.9, 20.2]	1.0 [-14.0, 15.9]
CG	126.5±46.0	117.6±51.3	119.0±36.5	-8.9 [-21.4, 3.6]	-7.5 [-17.0, 1.9]	1.3 [-5.1, 7.8]
Muscle Thickness, mm						
RTG	71.6±8.0	77.4±7.3	78.2±6.3	5.8 [-0.2, 11.8]	6.6* [1.7, 11.6]	0.8 [-7.2, 8.8]
ACG	68.2±19.0	71.2±19.3	72.5±19.4	2.9 [-3.5, 9.4]	4.3 [-0.5, 9.2]	1.4 [-1.9, 4.6]
CG	66.3±9.3	65.7±9.6	66.9±10.0	-0.7 [-4.7, 3.4]	0.6 [-3.3, 4.5]	1.2 [-2.9, 5.3]
Muscle Quality (echo intensity), a.u.						
RTG	19.0±3.1	19.0±5.4	19.0±3.4	0.2 [-2.9, 3.4]	-0.1 [-2.8, 2.7]	-0.3 [-3.8, 3.2]
ACG	21.0±5.5	17.4±5.0	18.9±4.8	-3.6 [-6.3, -1.0]	-2.1 [-5.6, 1.3]	1.5 [-1.1, 4.0]
CG	22.1±5.8	19.3±2.4	20.3±5.3	-3.1 [-7.3, 1.2]	-1.9 [-6.6, 2.9]	1.2 [-5.5, 8.0]

[Resistance training effects on muscle strength and muscle mass]

Results: No differences at baseline were observed between groups for

any of the outcomes. The RET group was significantly superior than CG group for muscle strength (+13.6 N.m, 95% CI: 5.8 to 21.3 N.m; $P = 0.001$) and muscle thickness (+4.3 mm, 95% CI: 1.4 to 7.2 mm; $P = 0.003$), and no differences were observed for muscle quality ($P = 0.414$). Although a superiority was found for RET when compared to ACG on the outcomes, no statistical difference was found ($P = 0.222 - 0.408$).

Conclusion: Resistance training is likely to be an effective tool to enhance physical function and musculoskeletal system in compensated cirrhotic patients. Greater sample sizes will be necessary to determine the superiority of resistance training in future studies.

Disclosure: Nothing to disclose

P0911

INFERIOR VENA CAVA COLLAPSIBILITY AS A PREDICTOR OF MORTALITY AND COMPLICATIONS IN PATIENTS WITH ACUTE VARICEAL UPPER GASTROINTESTINAL BLEEDING

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Introduction: Proper initial resuscitation is one of the first steps in the management of patients with acute variceal upper gastrointestinal bleeding (AVUGIB). Measurement of inferior vena cava (IVC) collapsibility by point-of-care ultrasound (POCUS) is a non-invasive tool to assess the response to fluid administration.

Aims & Methods: Our aim was to determinate the usefulness of measuring the IVC collapsibility by POCUS in patients with AVUGIB. This is a single-center prospective study. We included spontaneously breathing patients with AVUGIB from April to October 2019 who underwent upper endoscopy.

We excluded patients under the age of 18, previously treated at another institution, pregnant subjects, or patients with cardio-pulmonary diseases. IVC collapsibility was obtained 3 cm caudal from the right atrium and IVC junction using POCUS. IVC collapsibility was measured upon admission prior to resuscitation, ten minutes before endoscopy, and 24 hours after endoscopy.

The patients received standard treatment for AVUGIB by the attending physician. We analyzed the correlation of IVC collapsibility with re-bleeding at 5 days or 6 weeks, intubation, use of vasopressors, days of hospitalization and in-hospital mortality.

Results: We included 40 patients. There were 33 (82.5%) men, with a median age of 55.87 ± 10.87 years (SD), 17 (42.5%) patients had a previous event of AVUGIB. Etiology of cirrhosis was alcohol in 29 (72.5%) patients. Fourteen (35) patients had Child-Pugh A cirrhosis, 20 (50%) B and 6 (15%) C. The median MELD score was 14.15 ± 5.08 (SD). Most patients had esophageal variceal bleeding [32 (80%)]. Of the 40 patients, 14 had IVC collapsibility at admission. When comparing the clinical outcomes of patients admitted with IVC collapsibility versus those without collapsibility (Table 1), we observed a greater need for transfusions in patients with IVC collapse [13 (59.1) vs 9 (40.9), $p = 0.001$]; as well as greater need for vasopressors [5 (100) vs 0 (0), $p = 0.003$], and intubation [6 (100) vs 0 (0), $p = 0.001$]. We found higher in-hospital mortality in those admitted with IVC collapsibility [5 (100) vs 0 (0) $p = 0.003$]. There was no difference in days of hospitalization, nor rate of re-bleeding at 5 days or 6 weeks.

	IVC collapsibility n = 14	Non-IVC collapsibility n = 26	P
MELD $\pm$ SD	14.79 $\pm$ 5.53	13.69 $\pm$ 4.83	0.628
MELD Na $\pm$ SD	16.64 $\pm$ 5.19	15.31 $\pm$ 6.69	0.261
Transfusion (%)	13 (59.1)	9 (40.9)	0.001
Pre-Endoscopic (%)	10 (66.7)	5 (33.3)	0.002
Post-Endoscopic (%)	10 (62.5)	6 (37.5)	0.006
Re-bleeding at 5 days (%)	2 (100)	0 (0)	0.117
Re-bleeding at 6 weeks (%)	4 (66.7)	2 (33.3)	0.154
Need for Intubation (%)	6 (100)	0 (0)	0.001
Need for vasopressors (%)	5 (100)	0 (0)	0.003
In-hospital mortality (%)	5 (100)	0 (0)	0.003
Days of hospitalization $\pm$ SD	6.43 $\pm$ 5.787	4.38 $\pm$ 0.85	0.401

IVC: inferior vena cava

[Table 1. Clinical outcomes comparing patients with IVC collapsibility versus Non-collapsibility]

Conclusion: The measurement of IVC collapsibility by POCUS is useful to predict need for transfusions, vasopressors, intubation, and mortality in patients with AVUGIB.

Disclosure: Nothing to disclose

P0912

ASCITIC FLUID ANALYSIS IN REFRACTORY ASCITES UNDERGOING THERAPEUTIC PARACENTESIS: WORTH THE EFFORT?

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Introduction: Spontaneous bacterial peritonitis (SBP) is a common complication of advanced cirrhosis with a mortality rate of 20% with early diagnosis and treatment. The cell count and differential of the ascitic fluid (AF) is mandatory for inpatients with cirrhosis decompensation. However, the recommendations for outpatients with refractory ascites undergoing therapeutic paracentesis are controversial. While AASLD recommend testing outpatients AF for cell count and differential; EASL suggests testing only AF for new onset of ascites and cirrhosis decompensation, missing a recommendation for asymptomatic outpatients doing therapeutic paracentesis.

Aims & Methods: We aimed to assess the prevalence of SBP and bacterascites in asymptomatic outpatients under therapeutic paracentesis. We retrospectively included all the therapeutic paracentesis performed in asymptomatic outpatients between February and October of 2019. The cell count and differential, albumin and total protein concentration and culture of the AF were assessed. The outcomes were the diagnosis of SBP or bacterascites and the diagnosis of SBP or hospitalization within one month after paracentesis.

Results: We assessed 101 therapeutic paracentesis corresponding to 22 outpatients. Of the 22 cirrhotic patients, 18 were Child-Pugh B and 4 were Child-Pugh C. All patients were asymptomatic at the time of therapeutic paracentesis and 4 patients were under SBP prophylaxis. Of the 101 therapeutic paracentesis, all had elevated serum albumin ascites gradient (SAAG) indicating portal hypertension and 32 had total protein of AF < 1.5g/dL. In no case, AF fulfilled the criteria for SBP or AF culture was positive. No therapeutic paracentesis was associated with further diagnosis of SBP within one month of paracentesis. In 21 therapeutic paracentesis the patient was admitted to the hospital due to cirrhosis decompensation unrelated to paracentesis and within one month of paracentesis (2 hepatic encephalopathy; 6 ascites with hepatic encephalopathy, 5 urinary infection, 4 community-acquired pneumonia, 2 acute renal injury, 2 gastrointestinal bleeding), but no death within one month of paracentesis was documented.

Conclusion: Despite the retrospective design, the study suggests that the routine ascitic fluid analysis in refractory ascites undergoing therapeutic paracentesis does not have clinical impact, allowing better medical resources allocation.

Disclosure: Nothing to disclose

P0913

RESISTANCE TRAINING EFFECTS ON QUALITY OF LIFE AND FATIGUE FOR COMPENSATED CIRRHOTIC PATIENTS: PRELIMINARY RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Introduction: Cirrhosis has been associated with sarcopenia, which might impair prognosis, cause chronic fatigue and diminish quality of life. Resistance training (RT) is able to increase muscle mass in elderly patients. Therefore, it is expected that it might improve clinical outcomes in cirrhotic patients.

Aims & Methods: The aim of the present 3-arm randomized controlled trial is to verify the safety and the efficacy of RT to improve fatigue and quality of life for compensated cirrhotic patients.

Twenty compensated cirrhotic patients Child-Pugh A or B were recruited to the study. After completion of the baseline assessment, participants were randomly assigned to 3 groups: resistance training group (RET; n = 7), active control group (ACG; n = 6) and control group (CG; n = 7). ACG group undertook a low-intensity stretching and walking program once a week, while the CG group underwent monthly clinical follow-up for 24 weeks. RET group performed two weekly RT sessions, with an average duration of 50 minutes and an interval of 48 hours between sessions. Patients were followed up in weeks 0, 6, 12 and 24. Clinical scores regarding quality of life for chronic liver disease (CLDQ¹), quality of life regarding outcomes (SF-36²) and fatigue were performed (EICF³). In these visits, clinical and laboratorial data were gathered in order to analyze safety of RT. Data is presented as descriptive of the means of each group.

Results: Clinical variables did not change over the course of RT in all groups. Liver-specific scores, such as Child-Pugh and MELD remained stable for the follow-up period. No decompensation of cirrhosis occurred, except for one death due to sepsis in the CG.

Fatigue as measured by the EICF decreased in the follow-up - 37% improvement in RET, 15% improvement in ACG and 5% worsening in CG.

Quality of life as measured by the CLDQ questionnaire showed an improvement of 32% in RET, 10% in ACG and 14% in CG. Quality of life as measured by the SF-36 is divided in eight axis: physical limitation improved 100% in RET, 28.5% in ACG and worsened 0.9% in CG. Pain sensitivity improved 101% in RET, 21% in ACG and worsened 8.7% in CG. Functional capacity for daily activities improved 30.5% in RET, 5.3% in ACG and worsened 8.6% in CG. Vital individual perception improved 31.1% in RET, 2.1% in ACG and 6.4% in CG. Mental health evaluation improved 22% in RET, 5.1% in ACG and worsened 3.5% in CG. Social life perception improved 20% in RET, 18.5% in ACG and 4% in CG. Limitation with emotional background improved 49% in RET, 50% in ACG and 250% in CG. Self-evaluation of health status improved 9.5% in RET, 12% in ACG and 17% in CG.

Conclusion: RT for 24 weeks in compensated cirrhotic patients has been shown to improve quality of life and fatigue. This study is planned to be continued for another 18 months to include more patients.

Variable	Week 0	Week 24
Child-Pugh	RET 5 / ACG 5 / CG 5	RET 5 / ACG 5 / CG 5
MELD	RET 6 / ACG 8 / CG 6.8	RET 6.5 / ACG 9 / CG 7.8
MELD-Na	RET 8.3 / ACG 8 / CG 8.4	RET 7.3 / ACG 9 / CG 8.8
EICF	RET 44% / ACG 24% / CG 47%	RET 32% / ACG 21% / CG 49%
CLDQ	RET 4.9 / ACG 6.1 / CG 5.1	RET 6.5 / ACG 6.7 / CG 5.8
SF-36 Physical limitation	RET 50% / ACG 50% / CG 43%	RET 100% / ACG 100% / CG 31%
SF-36 Pain sensitivity	RET 36% / ACG 63% / CG 57%	RET 74% / ACG 76% / CG 52%
SF-36 Functional capacity	RET 73% / ACG 93% / CG 72%	RET 96% / ACG 98% / CG 66%
SF-36 Emotional limitations	RET 66% / ACG 66% / CG 16%	RET 100% / ACG 100% / CG 58%
SF-36 Vitality	RET 56% / ACG 78% / CG 38%	RET 73% / ACG 80% / CG 41%
SF-36 Mental Health	RET 59% / ACG 77% / CG 56%	RET 72% / ACG 81% / CG 54%
SF-36 Social aspects	RET 84% / ACG 83% / CG 78%	RET 100% / ACG 100% / CG 81%
SF-36 General Health	RET 78% / ACG 68% / CG 43%	RET 71% / ACG 60% / CG 36%

[Resistance training effects on improvement in quality of life and fatigue]

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Disclosure: Nothing to disclose

P0914

MELD SCORE AND ALBI GRADE ARE ASSOCIATED WITH POST-BANDING ULCER BLEEDING FOLLOWING ENDOSCOPIC VARICES LIGATION IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Acute esophageal varices bleeding is a severe and lethal complication of portal hypertension in patients with liver cirrhosis. Endoscopic varices ligation (EVL) has been recommend for prevention of esophageal varices bleeding as well as emergent treatment for acute esophageal varices bleeding.

However, following EVL, post-ligation ulcer may lead to another lethal bleeding episode. Data about predictive factors of post-banding ulcer bleeding (PBUB) is limited.

Aims & Methods: The aim of this study is to evaluate the predictors of PBUB following EVL. Patients underwent EVL were retrospectively evaluated in a tertiary medical center of northern Taiwan from Jan 2015 to Oct 2017. The PBUB was defined as upper gastrointestinal bleeding episode with upper endoscopy evaluation within 2 weeks after EVL. The demographic, clinical and endoscopic data were collected at the time of EVL. Categorical variables were compared by using Chi-square test and continuous variables were compared by using the Student t test. Univariate and multivariate logistic regression was performed to determine the predictive factors or models of PBUB.

Results: A total of 713 patients were enrolled in this study. 41 (5.8%) patients suffered from PBUB. The non-PBUB group was significantly older than PBUB group (58.35±12.48 vs 53.95±11.53, $p=0.028$). The prothrombin time, total bilirubin, ALT were significantly higher in PBUB group than those in non-PBUB group and albumin was significantly lower in PBUB group than that in non-PBUB group.

In univariate analysis, the prothrombin time (INR) >2.3, total bilirubin >3.0 mg/dl, sodium >150 mEq/L, MELD score ≥ 20 and ALBI grade 3 were associated with PBUB. In multivariate analysis, the MELD score ≥ 20 and ALBI grade 3 concomitant gastric varices were associated with the PBUB.

Conclusion: Concomitant gastric varices with MELD score ≥ 20 as well as ALBI grade 3 were independent predictors for the development of PBUB.

Disclosure: Nothing to disclose

P0915

SPLEEN STIFFNESS MEASUREMENT PREDICTS THE DEVELOPMENT OF PRIMARY HEPATOCELLULAR CARCINOMA BETTER THAN HEPATIC VENOUS PRESSURE GRADIENT

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Introduction: Hepatocellular carcinoma (HCC) is one of the main complications of chronic liver diseases. Recently, the degree of portal hypertension (PH) has been associated with HCC development. The gold standard method to evaluate PH is the measurement of hepatic venous pressure gradient (HVPG), which is an invasive and risky method. In addition, several authors reported that liver and spleen stiffness measure-

ment (LSM and SSM) are good surrogate non-invasive test (NIT) of PH and its complications. To date, no data are available on the role of SSM in predicting HCC.

Aims & Methods: The aim of this study is to evaluate the predictive role of LSM, SSM and HVPG for HCC development in patients with compensated advanced chronic liver diseases (cACLD). We retrospectively collected data from patients with cACLD undergone LSM, SSM and HVPG examination within 6 months from transient elastography referred to our center between 2008 and 2018. Patients without at least one-year follow-up, with incomplete records or a previous HCC were excluded. A Spearman's test to evaluate collinearity between SSM and HVPG was performed. We performed a univariate analysis to evaluate the predictive role of HVPG, LSM, SSM and other NITs for PH evaluation for the development of HCC. We performed two different multivariate analysis alternatively using SSM or HVPG as markers of PH.

Results: Data of 200 patients which fulfilled inclusion criteria were retrospectively collected, of whom 21 developed CE. One-hundred and thirty (130) patients were males (67%). The median age of patients was 57 years. The main etiology of cACLD was hepatitis C virus (84.4% in patients without HCC and 95% in patients with). SSM and HVPG were confirmed to be collinear (Spearman's $Rho=0.594$, $p<0.001$). At univariate analysis the platelet count, LSM, SSM, HVPG, and other NITs (Fib-4, LSPS and PSR) were independently associated with HCC development. At multivariate analysis only the SSM [subdistribution hazard ratio (SHR) 1.112, 95% confidence interval (CI) 1.067-1.160, $p<0.001$] was an independent predictors of HCC development (Wald χ^2 24.8). In the second multivariate replacing SSM with HVPG, the platelet count (SHR 0.979, CI 0.965-0.994, $p=0.007$) and the LSM (SHR 1.032, CI 1.005-1.061, $p=0.019$) were independent predictors of HCC development (Wald χ^2 12.8).

Conclusion: SSM is able to predict the development of HCC in cACLD patients, better than HVPG and of the combination of LSM and platelet count.

Disclosure: Nothing to disclose

P0916

SPLEEN STIFFNESS MEASUREMENT FOR ASSESSING THE RESPONSE TO β -BLOCKERS THERAPY FOR HIGH-RISK ESOPHAGEAL VARICES PATIENTS

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Introduction: Non-selective β -blockers (NSBB) therapy is the treatment of choice for primary prophylaxis of cirrhotic patients with high-bleeding risk esophageal varices (HRV). The hemodynamic response to NSBB is assessed by the measurement of the hepatic venous pressure gradient (HVPG). Recently, liver and spleen stiffness measurement (LSM and SSM) were proposed as non-invasive surrogates of HVPG.

Aims & Methods: We aimed to evaluate LSM and SSM changes for assessing hemodynamic response in these patients. Cirrhotic patients and HRV were prospectively enrolled and evaluated at our Department before starting NSBB and after 3 months. Correlation between changes (delta) of HVPG after NSBB treatment and those of LSM or SSM by transient elastography were performed.

Results: From the initial 59 patients considered for the study, 20 were finally included in the analysis. Fifteen (15) patients reached hemodynamic response to NSBB according to HVPG. Changes in LSM did not correlate with changes in HVPG ($r=0.107$, $p\text{-value}=0.655$), unlike changes in SSM ($r=0.784$, $p\text{-value}<0.0001$). Delta SSM presented excellent accuracy in identifying HVPG responders (AUROC 0.973; 95% CI 0.912-1). The best cut-off for delta SSM to identify responders was -10% (sensitivity 100%, specificity 60%, NPV 100% and PPV 90%).

Conclusion: SSM could be a reliable non-invasive test for the assessment of hemodynamic response to NSBB therapy as primary prophylaxis for HRV. Similar to HVPG, an SSM reduction $\geq 10\%$ is able to assess hemodynamic response.

Disclosure: Nothing to disclose

P0917

RESULTS OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IN THE TREATMENT OF REFRACTORY ASCITES

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Introduction: Transjugular intrahepatic portosystemic shunt (TIPS) is used to treat refractory ascites in cirrhotic patients who are not eligible for orthotopic liver transplant or as a bridge to transplant treatment.

Aims & Methods: To evaluate the safety and efficacy of TIPS in the treatment of refractory ascites.

Retrospective observational study of patients who underwent TIPS for refractory ascites, between 2015 and 2019. The clinical response was classified as: absent (need for paracentesis), partial (need for diuretics) or complete (no need for treatment).

Results: Thirty eight patients were included (65.8% were men, mean age 58 years). Twenty five patients (65.8%) had alcoholic cirrhosis and 5 patients (13.2%) cirrhosis due to alcohol + hepatitis C virus infection. The median follow-up time was 7.5 months.

The median values of MELD, MELD-Na and Child-Pugh (CP) scores were 13, 17 and 8, respectively. Three patients (7.9%) had a grade I hepatic encephalopathy (HE). Seventeen patients (44.7%) were listed for transplant. Pre and post-TIPS mean portosystemic pressure gradient (PPG) was 19.0 ± 1.1 and 6.9 ± 0.6 , respectively.

There was a complete response in 11 patients (28.9%), partial response in 18 patients (47.4%) and an absent response in 9 patients (23.7%). There were no significant correlations between clinical response and pre-TIPS MELD, MELD-Na or CP values, inferior vena cava or portal vein pressure values, nor pre or post-TIPS PPG.

After the procedure, HE worsening was verified in 23 patients (60.5%). Other complications occurred in 5 patients (13.2%): sepsis ($n=2$), capsular perforation ($n=1$), portal thrombosis ($n=1$) and hemolytic anemia ($n=1$). Nine patients (32.7%) died. Mortality correlated with a higher CP score value ($p=0.013$) and the presence of pre-TIPS HE ($p=0.01$). Thirty day mortality was 7.9% ($n=3$).

Conclusion: TIPS improves ascites management in the majority of patients, as it increases the incidence of HE. No adequate predictors of clinical response were found.

Disclosure: Nothing to disclose

P0918

PHYSICAL REHABILITATION IN THE CIRRHOTIC PATIENT: RESULTS FROM A CLINICAL TRIAL

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Introduction: Cirrhotic patients have reduced functional condition, exercise capacity and respiratory muscle strength, contributing to a greater state of physical inactivity, further worsening the functional condition and quality of life of these patients. Advanced liver disease is capable of causing a level of physical disability sufficient to generate chronic fatigue. A rehabilitation program could stimulate the practice of exercises, improving the functional condition, reducing fatigue and improving quality of life. Thus, it would allow these individuals to present better physical condition and longer survival.

Aims & Methods: The aim of this clinical trial is to assess functionality, respiratory and peripheral muscle strength, fatigue, physical and functional variables before and after an aerobic exercise program in cirrhotic patients.

This study is part of a randomized clinical trial registered at the Brazilian Clinical Trials Platform (REBEC-RBR3ftcvj) and approved by the Research Ethics Committee of the Federal University of Health Sciences of Porto Alegre - UFCSPA and Irmandade Santa casa de Misericórdia de Porto Alegre - ISCMPA-RS, Brazil (No. 3805918 and 3938979, respectively). Patients with compensated cirrhosis underwent an aerobic exercise program (treadmill and exercise bike) for one month, twice a week for 1 hour. Patients were assessed in the pre and post intervention periods for respiratory muscle strength (manuvacuometry) and peripheral muscle (translated by peak flexion torque and quadriceps extension on the dominant side), fatigue (Fatigue Severity Scale) and functional capacity (Test 6-minute walk - 6MWT). Correlations were assessed with Spearman's Correlation Coefficient and Wilcoxon Test was used for nonparametric variables. The p-value was considered significant when $< 0,05$.

Results: The sample consisted of 12 patients, 50% male, with a mean age of $57,83 \pm 8,84$ years, 41,7% with cirrhosis due to hepatitis C virus, body mass index (BMI-Kg / m²) average of $30,32 \pm 4,98$, average MELD of 11. Only 25% performed some physical activity regularly. Table 1 shows the behavior of the other variables between the periods before and after the exercise program.

Variable	Pre exercise program		Post exercise program		p
	Mean	Std. Deviation	Mean	Std. Deviation	
6-minute walk test	469.8	59.4	495.0	62.4	0.04
Fatigue	3.9	1.3	3.0	1.4	<0.01
Maximum inspiratory pressure (Pimax)	71.5	24.8	72.8	23.5	0.30
Maximum expiratory pressure (Pemax)	110.8	25.7	115.4	26.6	0.04
Peak torque flexion	45.6	22.9	53.1	28.4	0.07
Peak torque extension	121.8	48.1	126.4	74.6	0.23

[Functionality, fatigue, respiratory and peripheral muscle strength before and after the aerobic exercise program]

Conclusion: Patients showed increased functionality and maximum expiratory pressure, as well as reduced fatigue, a factor that contributes to physical inactivity. Although the exercise program was short-lived, it was

sufficient to positively impact the physical condition of these individuals. Muscle strength did not increase significantly after one month, but it showed this trend. A more extensive exercise program and loaded exercises can further contribute to improving the physical and functional condition of these patients.

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Disclosure: Nothing to disclose

P0919

THE EFFECT OF SGLT2 INHIBITORS/GLP1 RECEPTOR AGONISTS ON LIVER CIRRHOSIS IN NAFLD AND NASH COMPARED TO METFORMIN OR THIAZOLIDINEDIONES: A NATIONAL DATABASE STUDY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a growing pandemic health issue and medical problem. It is most commonly associated with insulin resistance, obesity and type 2 diabetes (T2DM). It can progress to non-alcoholic steatohepatitis (NASH) which can lead to liver cirrhosis (LC) and, in some cases, to hepatocellular carcinoma. Currently, there are no approved treatments for NAFLD/NASH, other than life-style changes. GLP-1 receptor agonists (GLP-1 RA) and SGLT2 inhibitors (SGLT2i) are both known to induce weight loss by various mechanisms. Recent small studies have shown some efficacy of GLP-1 RA and SGLT2i on regression of NAFLD/NASH in patients with T2DM.

Aims & Methods: **Aim:** To examine if patients with NAFLD/NASH on SGLT2i and/or GLP-1 RA have a reduced risk of being diagnosed with LC when compared to those on metformin alone or thiazolidinediones (TZD) alone. **Methods:** Using a large commercial medical database (IBM Explorys Solutions, IBM, Inc.), we identified cases, defined as adult patients with NAFLD/NASH who were using either SGLT2i or GLP-1 RA or both for at least 1 year before getting a new diagnosis of LC.

Explorys utilizes the Systematized Nomenclature of Medicine - Clinical Terms (SNOMED - CT) system to code variables, including drugs and diagnoses. Control group 1 were adult patients with NAFLD/NASH using Metformin for at least 1 year before being diagnosed with LC. Control group 2 comprised of NAFLD/NASH patients on TZD for at least 1 year before being diagnosed with LC. Odds ratios (OR) and 95% confidence intervals (CI) for the OR were calculated for the comparative odds of receiving a new diagnosis of LC in cases vs. controls.

Results: From a total of 64,417,480 patients in the Explorys database, we identified 53,690 patients with NAFLD/NASH on SGLT2i/GLP-1 RA (cases), 1,741,980 on Metformin (control group 1), and 80,250 on TZD (control group 2). Baseline demographics of the three groups are shown in Table 1.

When compared to controls on metformin, cases on SGLT2i/GLP-1 RA were significantly less likely to receive an incident diagnosis of LC (OR: 0.21, 95% CI: 0.15-0.31). Similarly, when compared to controls on TZD, cases on SGLT2i/ GLP-1 RA were significantly less likely to have a new diagnosis of LC (OR: 0.22, 95% CI: 0.13-0.38).

In a sensitivity analysis, both SGLT2i and GLP-1 RA were independently associated with a lower risk of receiving a new diagnosis of LC, although the relative risk reduction was stronger in the GLP-1 RA when compared to the SGLT2i (Table 2).

	Case (GLP/SGLT) N = 850	Control 1 (Metformin) N = 11,210	Control 2 (Glitazones) N = 320
Age (18 - 65 years)	72.9%	57.9%	40.6%
Age > 65 years	25.9%	42.2%	62.5%
White race	88.2%	86.4%	87.5%
African American race	5.9%	5.7%	6.3%
Female gender	63.5%	62.0%	53.1%
Male gender	36.5%	38.0%	46.9%
Diabetes mellitus type 2	90.6%	90.6%	87.5%
Smoking history	23.5%	25.4%	21.9%
Obesity (BMI > 30)	60.0%	53.5%	43.8%

[Table 1: Baseline demographics of the cases and controls]

	Case (Risk %)	Control (Risk %)	OR	95% CI
GLP/SGLT vs Metformin	30 (4.05%)	690 (16.51%)	0.21	0.15-0.31
GLP/SGLT vs Glitazones	30 (4.05%)	30 (15.79%)	0.22	0.13-0.38
GLP vs Metformin	25 (4.85%)	690 (16.51%)	0.25	0.17-0.39
SGLT vs Metformin	5 (1.64%)	690 (16.51%)	0.08	0.03-0.20
GLP vs Glitazones	25 (4.85%)	30 (15.79%)	0.27	0.15-0.47
SGLT vs Glitazones	5 (1.64%)	30 (15.79%)	0.09	0.03-0.23

[Table 2: Risk of new diagnosis of liver cirrhosis in Cases vs. Controls]

Conclusion: Treatment with SGLT2i or GLP-1 RA decreases the incident risk of LC by ~ 80% when compared to either Metformin alone or TZD alone in patients with NAFLD/NASH. The retrospective design, small sample size and lack of histopathologic confirmation are limitations. Large randomized controlled trials and prospective studies are needed to confirm these findings.

Disclosure: Nothing to disclose

P0920 WITHDRAWN

P0921

LYMPHOCYTE TO MONOCYTE RATIO CAN BE A SIMPLE AND NOVEL PREDICTOR IN CIRRHOTIC PATIENTS WITH CULTURE NEGATIVE NEUTROCYTIC ASCITES

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Introduction: Spontaneous bacterial peritonitis (SBP) is a serious common form of infection in cirrhotic ascitic patients. Ascitic fluid infection consists primarily of two variants, namely, culture-negative neutrocytic ascites (CNNA) and SBP. There are so many inflammatory markers were defined in ascitic fluid infection.

Aims & Methods: The aim of our study was to compare the inflammatory markers between cirrhotic ascitic patients without ascitic fluid infection and culture-negative neutrocytic ascites. Beside that we aim to compare and evaluate the clinical utility of this inflammatory markers and non-invasive tests between diagnosis and after the treatment. A total of 123 cirrhotic ascitic patients were included in this study. The diagnosis of cir-

rhosis was made on the basis of clinical, biochemical, ultrasonic, histological, and endoscopic findings. Twenty ml of ascitic fluid was taken under complete aseptic technique, from a puncture site, by paracentesis. 10 ml was immediately inoculated in bedside aerobic and anaerobic blood culture bottles. The remaining amount of ascitic fluid was sent for biochemical and cytological examination in tubes containing EDTA and analyzed within 2 hours of aspiration.

According to international guidelines, CNNA was diagnosed if the polymorph nuclear neutrophil (PMN) cell count in the ascitic fluid $\geq 250/\text{mm}^3$ in the absence of other causes of peritonitis, but without a positive culture in the appropriate setting, which includes: The fluid must be cultured in blood culture bottles, no previous antibiotic therapy, and no other explanation for an elevated PMN count. Finally we check the patient ascite on the fifth day of treatment for recovery.

Results: We analyzed 123 cirrhotic ascitic patients, 59 of them were CNNA (group A) and 64 of them were used as controls without ascitic fluid infection (group B). Group A and group B were matched for age, sex, MELD, CHILD, ascite and blood biochemical parameters. Also we compared the two groups for serum inflammatory markers. We found a significant differences for ascite lactate dehydrogenase (LDH), neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR) and C-reactive protein (CRP) ($p < 0,001$) between two groups.

Also we found a significant difference for white blood cell (WBC), neutrophil and monocyte count ($p < 0,05$). Following this we distinguish group A to before treatment and after treatment group. When we compare this two groups we found a significant differences between MPV count ($p < 0,05$), monocyte count, LMR and CRP level ($p < 0,001$).

	Before treatment	After treatment	P value
WBC ($10^3/\mu\text{l}$)	8,56 $\pm$ 5,73	7,87 $\pm$ 5,43	0,327
Neutrophil ($10^3/\mu\text{l}$)	6,56 $\pm$ 5,43	5,94 $\pm$ 4,54	0,304
Monocyte ($10^3/\mu\text{l}$)	0,67 $\pm$ 0,38	0,48 $\pm$ 0,25	<0,001
Lymphocyte ($10^3/\mu\text{l}$)	0,96 $\pm$ 0,53	0,98 $\pm$ 0,54	0,760
NLR	8,7 $\pm$ 7,18	7,58 $\pm$ 6,08	0,130
NMR	12,72 $\pm$ 11,25	14,92 $\pm$ 11,73	0,180
LMR	1,50 $\pm$ 0,43	2,09 $\pm$ 0,53	<0,001
MPV (fL)	10,01 $\pm$ 1,20	9,64 $\pm$ 1,44	0,004
CRP (mg/l)	72,01 $\pm$ 58,45	29,30 $\pm$ 30,83	<0,001

[Comparison between before and after the SBP treatment]

Conclusion: Monocyte count, LMR and CRP level could be used as a novel, simple, low cost, non-invasive test for diagnosis and treatment response of CNNA patients.

Disclosure: Nothing to disclose

P0922

MALNUTRITION AND MORTALITY RISK IN LIVER CIRRHOSIS PATIENTS

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Introduction: Malnutrition is a prevalent complication of liver cirrhosis (LC). This condition occurs in 20% of compensated patients and in more than 60% of patients with advanced LC. In order to provide a better service to the patient it is essential for health professionals to be aware of this major condition. Therefore, a malnutrition risk screening followed by a nutritional assessment should be performed.

Aims & Methods: The aim of this study was to assess the impact of malnutrition risk and malnutrition in the survival of LC patients.

The study occurred between January of 2018 and August of 2019 at a hepatology unit of a Portuguese hospital. Malnutrition risk was assessed through the Royal Free Hospital Nutrition Prioritizing Tool (RFH-NPT), while the nutritional status was assessed with the Subjective Global Assessment (SGA). To analyse the impact of these parameters in the survival of LC patients a Cox regression was performed, and the results were adjusted to the concomitant presence of hepatocellular carcinoma (HCC), age, and Model For End-Stage Liver Disease score (MELD score).

Results: The sample was composed by 124 LC patients, 21% of whom had HCC. Patients were predominantly male (80.6%), with a mean age of 60.7 $\pm$ 10.8 years old, and a mean MELD score of 15.9 $\pm$ 7.2.

Most of the sample was at high risk of malnutrition (84/124, 67.7%), while 11.3% (14/124) were medium risk of malnutrition. The prevalence of malnutrition was 74.2% (92/124) and 3 patients at high risk of malnutrition were not assessed as malnourished.

In univariate analyses, high risk of malnutrition (HR= 3.861, $p = 0.01$), moderate malnutrition (HR= 3.649, $p = 0.008$) and severe malnutrition (HR= 3.846, $p = 0.008$) were associated with poor survival. Nevertheless, only high risk of malnutrition remained statistically significant (HR= 3.245, $p = 0.029$) after adjustment for other mortality risk factors, such as presence of hepatocellular carcinoma, age, and MELD score.

Conclusion: Patients at high risk of malnutrition had a 3-fold higher mortality risk than patients who were at low risk of malnutrition. These results suggest that after adjustments having a high risk of malnutrition was the best predictor of poor survival. Therefore, not only malnourished patients but also those with high risk of malnutrition should be followed closely in order to optimize their nutrition intake and reassess their nutritional status. The present study also reinforces that nutritional assessment is difficult in LC patients and new tools that consider these difficulties should be tested and validated with hard outcomes like mortality.

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Disclosure: Nothing to disclose

P0923

NON-ALCOHOLIC FATTY LIVER DISEASE INVOLVES DEVIATIONS IN MICRORNAS AND HEMATOLOGICAL INDICES - A SINGLE CENTRE OBSERVATION

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Introduction: MicroRNAs (miRNAs) belong to endogenous, short regulatory RNA molecules involved in the modulation of gene expression. They were found to participate in the progression of various liver pathologies, e. g. acute liver failure, alcohol-related liver disease and non-alcoholic fatty liver disease (NAFLD). On the other hand, there are attempts to verify the role of hematological indices in patients with liver disorders. All these efforts are made to broaden the spectrum of available noninvasive diagnostic tools in the course of liver pathologies.

Aims & Methods: Our goal was to assess the relationships between selected miRNAs and hematological indices in the course of NAFLD. One hundred ninety seven persons were enrolled to the study: 97 with NAFLD and 100 healthy volunteers in control group. Serological expression of miR-126-3p, miR-197-3p and miR-1-3p was evaluated in all examined patients. Hematological markers were also assessed: mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), mean platelet volume to platelet ratio (MPR) and platelet to lymphocyte ratio (PLR). Then correlations between evaluated indices were performed. A diagnostic value of miRNAs together with proposed cut-off in research group were measured with area under the curve (AUC).

Results: The expression of examined miRNAs (miR-126-3p, miR-197-3p and miR-1-3p) in NAFLD group differed significantly in comparison to controls; a concentration of miR-126-3p and miR-1-3p was higher and miR-197-3p - lower ($p < 0,0001$). Furthermore, miR-197-3p correlated positively with PLR and negatively with PDW ($p < 0,05$). MiR-126-3p turned out to be the most powerful diagnostic marker among assessed miRNAs in examined NAFLD group with AUC of 0,716 for the cut-off $>9,49$ amol/ μ l ($p < 0,0001$); AUC of miR-197-3p was 0,672 for the cut-off $< 0,32$ amol/ μ l ($p < 0,0001$).

Conclusion: According to available literature it seems that serological expression of miR-126-3p, miR-197-3p and miR-1-3p was explored mainly in patients with hepatocellular injury and hepatocellular carcinoma. To the best of our knowledge it appears to us that we present for the first time relationships between the above-mentioned miRNAs and hematological indices in the course of NAFLD. Further studies are required to explore this topic, however we suspect that certain serological miRNAs together with other blood parameters may become in the future the markers of NAFLD.

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Disclosure: Nothing to disclose

P0924

REAL WORLD EFFICACY AND SAFETY OF SOFOSBUVIR/LEDIPASVIR WITH OR WITHOUT RIBAVIRIN IN PATIENTS WITH DECOMPENSATED LIVER CIRRHOSIS AND HEPATITIS C VIRUS INFECTION: A COHORT STUDY

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Introduction: Sofosbuvir+Ledipasvir±Ribavirin showed good results in terms of efficacy and safety in clinical trials in advanced liver cirrhosis, but real life data are still needed in order to confirm this profile.

Aims & Methods: The aim of the present study was to investigate the efficacy and safety of Sofosbuvir+Ledipasvir±Ribavirin in a real- world large Romanian population with liver cirrhosis and genotype 1b hepatitis C virus.

We analyzed a multicentric retrospective cohort enrolling 349 patients with decompensated liver cirrhosis due to chronic hepatitis C who received Sofosbuvir+Ledipasvir±Ribavirin for 12/24 weeks (301/48). Patients were included between 2017-2018, all with genotype 1b. Main inclusion criteria were liver cirrhosis and detectable HCV RNA. The cases were followed-up monthly during therapy and 12 weeks after the end of therapy.

Results: The cohort included 60% females with a median age of 61, 16% Interferon pre-treated, 53% with co-morbidities, 40/53/7 % with Child Pugh (CTP) A/B/C, 4% with virus B co-infection and 8% with previously treated hepatocellular carcinoma. Mean initial MELD score was 11.92 (6.82÷ 24.5). Six patients were lost during follow-up and in 16 patients (4.6%) treatment was interrupted due to adverse events. Sustained viral response (SVR) in intention-to-treat analysis was reported to be 85.1% and 90.8% in per protocol analysis. Predictive factors of SVR in decompensated cirrhosis were: female gender ($p=0.01$), advanced age ($p<0.001$), lower bilirubin levels ($p=0.002$) and lower CTP score ($p=0.02$) (Table 1). In patients with Child Pugh B/C low bilirubin levels ($p=0.003$), low INR ($p<0.001$), increased platelet count ($p=0.04$), low CTP score ($p<0.001$), lack of encephalopathy ($p=0.02$), serum albumin >3.5 g/dl ($p=0.002$) predicted improvement of liver function.

Parameter	Responders	Non-responders	p-value
Age	61 (35÷83)	56 (37÷72)	<0.001
Male gender	38.4%	57.7%	0.014
Co-morbidities	52.5%	55.8%	0.764
CTP score	7(5÷11)	8(5÷12)	0.02
HCV-RNA	276000 (55 ÷ 7276049) IU/l	167000 (11400÷1970000)IU/l	0.311
Total bilirubin	1.5(0.3 ÷ 9) mg/dl	2.2 (0.4 ÷ 11) mg/dl	0.002
MELD	10.48 (6.14÷ 19.71)	10.48 (6.14÷ 19.71)	0.148
Ascites at therapy initiation	42.8%	42.3%	1.000
Variceal bleeding in patient's history	12.8%	17.3%	0.381

[Table 1. Predictive factors of SVR to Sofosbuvir+Ledipasvirin patients with decompensated liver cirrhosis (univariate analysis) by ITT]

Conclusion: Sofosbuvir+Ledipasvir±Ribavirin proved to be highly efficient in our difficult to treat population. SVR12 rates did not differ significantly between patients with treatment duration of 12 or 24 weeks,

and between those treated with Ribavirin or without. The main predictors of SVR were the advanced age and the lower bilirubin levels. 66% of patients had an improvement of their liver function after therapy, and Sofosbuvir+Ledipasvir±Ribavirin was very well tolerated in our difficult-to-treat cases, with serious adverse events reported in only 4.6% of cases, most of them represented by worsening of the liver function (9/16).

Disclosure: Nothing to disclose

P0925

PREVALENCE, RISK FACTORS AND CLINICAL IMPACT OF MULTIDRUG-RESISTANT BACTERIAL COLONIZATION IN CIRRHOTIC PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT IN A SPANISH TERTIARY HOSPITAL

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Introduction: The prevalence of infections caused by multidrug-resistant bacteria (MDR) is increasing in recent years both in the general population and in cirrhotic patients. Data on prevalence, risk factors and clinical impact of MDR bacterial colonization in the cirrhotic population are still limited. In addition, resistance patterns may vary between different areas and hospitals.

Aims & Methods: The primary aim of our study was to investigate the prevalence of MDR bacterial colonization in critical cirrhotic patients requiring admission to the Intensive Care Unit (ICU) of our hospital, to analyze the risk factors involved in colonization by these microorganisms and to evaluate its relationship with the development of intra-ICU MDR bacterial infection.

Retrospective study including all critical cirrhotic patients that required intensive care admission and underwent triple smear (nasal/pharyngeal/rectal) to investigate MDR bacterial colonization at admission to ICU, as part of the Zero Resistance (ZR) program. Patients were followed during their stay in ICU.

Results: Between March 2015 and December 2019, 302 patients with liver cirrhosis were admitted to the ICU at our centre. 117 (38.7%) underwent triple smears to investigate MDR bacterial colonization following the recommendations of the ZR program at our hospital. 28 of the 117 patients (23.9%) were colonized by one MDR bacteria and in 3 of them simultaneous colonization by 2 MDR bacteria was detected.

The most frequently isolated colonizing MDR bacteria were extended-spectrum beta-lactamase *Enterobacteriaceae* (ESBL) (45.2%), *Stenotrophomonas maltophilia* (25.8%), methicillin-resistant *Staphylococcus aureus* (16.1%), carbapenem-resistant *Pseudomonas aeruginosa* (3.2%) and other microorganisms (9.7%).

The presence of ≥ 3 risk factors of ZR checklist at ICU admission was significantly related to MDR bacterial colonization (40% vs 11.9%; $p=0.000$; OR 4.9 CI95% [1.9-12.5]). Other potential risk factors such as norfloxacin antibiotic prophylaxis, proton pump inhibitor consumption and the community origin of the patient, showed no significant association with the risk of colonization (35.3% vs 22%; $p=0.23$; 27.3% vs 17.5% $p=0.24$ and 26% vs 20.4% $p=0.49$, respectively). Incidence of intra-ICU MDR bacterial infection

was significantly higher in the group of patients colonized upon ICU admission (42.8% vs 16.8%; $p=0.004$; OR 3.7 [1.5-9.4]). In the colonized patients who developed infection, there was a 91.6% concordance between colonizing and infecting agents.

Conclusion: MDR bacterial colonization is common in patients with cirrhosis requiring ICU admission in our area. The presence of ≥ 3 items from the ZR checklist at admission is a risk factor for MDR bacterial colonization in this population. Basal colonization by MDR bacteria on admission to the ICU is associated with an increased risk of developing MDR bacterial infection, with a high correlation between the MDR colonizing and infecting agents. These findings could help to guide empirical antibiotic treatment in these patients if signs of infection are present.

Disclosure: Nothing to disclose

P0926

PHASE ANGLE AND CLINICAL OUTCOMES IN LIVER CIRRHOSIS

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Introduction: Nutritional assessment is particularly difficult in liver cirrhosis (LC). However, it has been recently found that phase angle (PA) is a good indicator of nutritional status and is associated with poor prognosis in LC. This PA success is mainly due to its independence in relation to the hydration level, unlike other traditional methods of nutritional assessment, such as body mass index. The cut-off point proposed for patients with LC is $PA \leq 4.9^\circ$.

Aims & Methods: The aim of this study was to assess the impact of PA on clinical outcomes in LC.

Data collection took place from January 2018 to August 2019. Patients were evaluated within the first 72 hours of hospitalization and PA was assessed by electrical bioimpedance. The clinical outcomes evaluated were the length of stay (LOS), number of readmissions at 6 months (R6m) and mortality.

Results: The sample consisted of 107 patients, predominantly male (81.3%) and with a mean age of 60.8 ± 10.6 years old. In addition to LC, 22.4% of patients also had hepatocellular carcinoma (HCC).

The sample was stratified according to the cut-off point of the PA ($PA \leq 4.9^\circ$ or $PA > 4.9^\circ$), and it was found that PA was a predictor of mortality independently of the presence of HCC and Model For End-Stage Liver Disease score ($HR = 2.4$, $p = 0.01$). In an adjusted model concerning only nutritional parameters, it was also found that having $PA \leq 4.9^\circ$ increased 2.9 times the risk of death ($HR = 2.9$, $p = 0.002$), regardless of appendicular muscle mass, handgrip strength, gait speed and mid-arm muscle circumference.

There was also a negative correlation between PA, LOS ($n = 107$, $r_s = -0.276$, $p = 0.004$) and MELD score ($n = 105$; $r_s = -0.426$; $p < 0.001$). No significant relationship was found between PA and R6m ($n = 85$; $r_s = -0.036$; $p = 0.753$).

Conclusion: This study confirms the potential that PA presents in the categorization of patients with LC, allowing the screening of those who need more aggressive nutritional support. However, more studies with larger

samples should be conducted to validate these findings and randomized controlled trials are warranted in order to understand if a personalized and more aggressive nutritional approach results in an increase in PA and consequently an enhancement in survival of LC patients.

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Disclosure: Nothing to disclose

P0927

OUTCOMES OF PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH CIRRHOSIS: DOES THE STENT TYPE MATTER?

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Introduction: Patients with cirrhosis have underlying coagulopathy that may impact their outcomes after percutaneous coronary intervention (PCI). PCI with stent placement in cirrhotics has been associated to higher morbidity and mortality. Previous data has proven that bare-metal stents (BMS) are safer in cirrhotics, but it is unknown if the cirrhosis status (compensated vs. decompensated) plays a role when deciding what stent to use. We aim to investigate if drug-eluting-stents (DES) have worse outcomes and higher rate of complications than BMS in cirrhotics.

Aims & Methods: The National Inpatient Sample (NIS) 2016 was queried using ICD-10CM/PCS codes for all discharges of adult patients with cirrhosis who underwent PCI with placement of DES and BMS. Patients were subsequently divided into compensated and decompensated cirrhosis as per the validated BAVENO Score. Primary outcome was in-hospital mortality. Secondary outcomes include: rate of post-procedural complications such as post-procedural bleeding, endotracheal intubation, acute kidney injury (AKI), shock, cardiac arrest, intra-aortic balloon pump (IABP) need, pericardiocentesis, IMPELLA, ECMO use, shock and sepsis. Length of stay (LOS), total hospital charges and hospital cost were calculated and Multivariate logistic regression analysis was performed to adjust for potential confounders.

Results: 447,545 PCIs were identified out of which 0.6% (n=2,325) were cirrhotics. 20% (n=474) were decompensated cirrhotics. Decompensated cirrhotics were more likely to be Hispanic [14.7% vs 11.1%; (P< 0.01)]. Both compensated and decompensated cirrhotics had higher rates of BMS placement than those without cirrhosis [aOR 1.57; (P< 0.01)]. There was no significant difference in mortality between BMS and DES in patients with compensated cirrhosis [aOR 0.80; (P=0.63)] and similar results were obtained in patients with decompensated cirrhosis [aOR 0.07; (P=0.07)]. DES was associated to higher LOS when compared to BMS in patients with decompensated cirrhosis [4.93; (P< 0.01)] and with higher total hospital costs [16,031.94; (P< 0.01)]. Decompensated cirrhotics with a DES had higher risk of post procedure bleeding when compared with BMS [aOR 4.22; (P< 0.01)].

Conclusion: Decompensated cirrhotics admitted to the hospital for PCI who receive a DES have a prolonged hospital LOS and have higher total hospitalization costs. This is likely driven by higher rates of post-procedur-

al bleeding, likely requiring further intervention to control the bleed. Bare-metal stents seemed to be safe for cirrhotics overall, and is not associated with higher mortality - even in decompensated cirrhotics. Randomized control trials could evaluate the safety of the different PCI stents in cirrhotics to better assess if one is preferred over the other

Disclosure: Nothing to disclose

P0928

VARICEAL RECURRENCE AFTER ERADICATION: WHICH ROLE OF NONINVASIVE SCORES?

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Introduction: Esophageal varices (EV) are a life-threatening complication of portal hypertension. Endoscopic variceal ligation (EVL) is the main instrumental treatment either on primary or secondary prophylaxis. But after varices eradication remains the risk of variceal recurrence (VR) and consequently the risk of bleeding. The aim of our study was to evaluate the recurrence rate of EV and to determine the predictive factors.

Aims & Methods: We performed a single-center retrospective study analyzing data all patients with cirrhotic PH undergoing EVL for primary or secondary prophylaxis during 2010 to 2017. Patients aged under 17 years, with hepatocellular carcinoma or treated by sclerotherapy were excluded. The noninvasive scores: platelet to spleen diameter (PSD), aspartate aminotransferase to alanine aminotransferase ratio (AAR), APRI, FIB-4, King's score, *Cirrhosis Discriminant Score* (CDS), Goteborg University Cirrhosis Index (Guci) and age to platelet index were calculated for each patients at the first EVL. Variceal recurrence was defined as an increase in EVs size to $\geq$ grade 1, or the development of bleeding from EVs. Biochemical, endoscopic and morphologic data were collected.

Results: Overall eighty-nine patients undergoing EVL were included with a sex ratio H/F of 1.02. The mean age was 55,93 $\pm$ 14.17 years. The main cause of portal hypertension was cirrhosis. A total of 267 EVL sessions were performed with an average number of banding sessions per patients of 3 sessions (1 - 7). EVL was done in purpose of secondary prevention of variceal bleeding in 89% of cases and for primary prevention in 11%. Eradication of varices was obtained in 88.8% of cases. Variceal recurrence occurred in 41.7% of patients after eradication. In univariate analysis secondary prophylaxis (p=0.017), portal thrombosis (p=0,03), (p=0.003), APRI (p=0,008), Fib-4 (p=0.014), King's score (p=0.031), Guci score (p=0,017) and PSD (p< 0.001) were significantly associated with VR. In multivariate analysis, PSD was the only noninvasive score independent factor associated with VR (OR 7.9; 95% CI [2,544-31,301], p= 0.002). The area under the curve (AUC) of PSD as predictor of VR was 0.786 (95% CI [0,676-0,897], p< 0,0001). The optimal cutoff value of PSD predicting VR was 513 (sensitivity 74%, specificity 75%).

Conclusion: In our study PSD is reliable noninvasive predictor for variceal recurrence. Thus, we propose a cutoff 513 of to identify patients with risk of VR in order to optimize screening after eradication. PSD is a promising marker, requiring more studies in order to be integrated into a new risk score of VR after eradication.

Disclosure: Nothing to disclose

P0929

PERFORMANCE OF CIRRHOSIS SEVERITY SCORES AND BLEEDING RISK SCORES IN PREDICTING THE MORTALITY IN ACUTE VARICEAL BLEEDING

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Introduction: Acute variceal bleeding (AVB) is a lifethreatening condition and serious complication of portal hypertension that could compromise the immediate prognosis of cirrhotic patients.

Aims & Methods: Our objective was to compare the performance of cirrhosis severity scores and bleeding risk scores in predicting six-week mortality in patients with AVB.

We performed a retrospective analysis of data from consecutive cirrhotic patients hospitalized for an AVB, recruited from January 2012 to December 2019. Cirrhosis severity scores (MELD, MELD-Na, CHILD-pugh(CP), Albumin-Bilirubin (ALBI), Platelet-albumin-bilirubin (PALBI) ,and Neutrophil-lymphocyte Ratio(NLR)) and bleeding risk scores (AIMS 65, APASL score and GB score) were calculated on admission.

Results: Overall 195 patients were included with an average age of 65.4 ±13.1 years and sex-ratio of 1.7. Viral origin was the most common etiology (53.9%). During follow-up, these patients were admitted 460 times to our service for decompensation of their disease. One hundred and forty three admissions were related to AVB (31.1%). The six-week mortality rate was 25.7%. A statistically significant association was noted between sex-week mortality and the following scores: MELD (p <0.001), MELD-Na (p <0.001), ALBI (p = 0.004, PALBI (0.01) and CP (p <0.001). NLR was not significantly associated with mortality (p = 0.06). Bleeding risk scores were also associated with sex-week mortality: AIMS65 (p = 0.001), APASL (p = 0.002) and GB score (p <0.001). GB score had the best area under the ROC curve (AUROC = 0.894) followed by AIMS65 (AUROC = 0.873), APASL (AUROC = 0.839) and MELD(AUROC= 0.778). At the cut-off of 12.5, the GB score had a sensibility and specificity of 81.8% and 82% respectively. For cirrhosis severity scores, MELD had a sensibility and specificity of 81% and 70.3% respectively at the cut-off of 16.5.

Conclusion: In our study, bleeding risk scores were better than cirrhosis severity scores in predicting six-week mortality in patients with AVB, in particular, the GB score at the cut-off of 12.5.

Disclosure: Nothing to disclose

P0930

EXTRAHEPATIC NEOPLASIA DURING CIRRHOSIS: PREVALENCE AND PROGNOSIS

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Introduction: Admittedly, hepatocellular carcinoma(HCC) is the most frequent tumor during cirrhosis, nevertheless, extrahepatic neoplasia(EHN) which could compromise the prognosis of the disease are poorly studied.

Aims & Methods: Our objective was to determine the prevalence of EHN and to assess their prognosis.

We performed a retrospective analysis of data from consecutive patients followed in our department for cirrhosis recruited from January 2012 to December 2019.

Results: A total of 195 patients were included with an average age of 65.4 ±13.1 years and sex-ratio of 1.7. The etiology of cirrhosis was dominated by viral hepatitis C (30.8%), viral hepatitis B (23.1%) and non-alcoholic steatohepatitis (13.3%). During an average follow-up period of 17.2 months [1-96], 24 patients had EHN with a percentage of 12.3%. They were 13 men and 11 women with an average age of 70.4 ± 14.8 years. The most common etiology of cirrhosis was viral hepatitis C (45.8%). Patients were classified by the Child-Pugh (CP) score: 11 patients CP A, ten CP B and three CP C. Breast tumor was the most frequent EHN (7 cases) followed by prostatic adenocarcinoma (3 cases), bladder tumor (2 cases) and pulmonary adenocarcinoma (2 cases). Only seven patients benefited from curative treatment. During follow-up, seven patients developed HCC (29.1%). A significant correlation was noted between the presence of EHN and the occurrence of hepatic encephalopathy(p=0.03), upper gastrointestinal bleeding (p=0.03) and bacterial infections(p< 0.05). A total of 13 patients (54.1%) died, including four directly related to complications of cirrhosis and nine related to the advanced stage of their neoplasia. Mortality was significantly correlated with the presence of EHN (p=0.006).

Conclusion: In our study, 12.3% of cirrhotic patients had EHN with gynecological neoplasias predominance. Since the one compromised the therapeutic management of the other, the association between EHN and cirrhosis had a poor prognosis with a high morbidity and mortality.

Disclosure: Nothing to disclose

P0931

THE PREVALENCE AND PROGNOSTIC IMPACT OF AUTOIMMUNE HEMOLYTIC ANEMIA IN CIRRHOTIC PATIENTS

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Introduction: Anemia is a common and multifactorial biological abnormality during cirrhosis that could worsen its prognosis. Autoimmune hemolytic anemia (AIHA) is an entity that has been little studied in patients with cirrhosis.

Aims & Methods: Our objective was to determine the prevalence of AIHA in cirrhosis and assess its prognostic impact.

This is a retrospective study including all cirrhotic patients followed in our department between January 2012 and December 2019. The diagnosis of AHAI was retained in front of a regenerative anemia with a positive direct coombs test and stigmata of hemolysis (free hyper bilirubinemia, elevated lactate dehydrogenase and collapsed haptoglobin) in the absence of other overt cause of constitutional or acquired hemolysis

Results: A total of 187 cirrhotic patients were included with an average age of 60.2 years [11-89] and a sex ratio (M / F) of 1.79. Thirteen patients had an AIHA or seven percent of patients. Anemia was normocytic in 77% of cases and macrocytic in 23% of cases. Five patients had a history of associated autoimmune pathologies (38.4%). The AIHA was more frequent in cases of cirrhosis of viral origin B and C (46.1%). Three patients had cirrhosis of non-viral origin (23%): primary biliary cholangitis, autoimmune hepatitis and alcoholic cirrhosis. The etiology of cirrhosis was unknown

in 30.7%. The AHAI was significantly correlated with the severity of cirrhosis estimated by the Child-pugh score ($p = 0.014$) and the MELD score ($p = 0.02$). A significant correlation was also noted between the AIHA and the oedematoascitic decompensation (OAD) ($p = 0.012$) and hepatic encephalopathy (HE) ($p = 0.009$). During the follow-up, five patients had died, giving a mortality rate of 38.4%.

Conclusion: In our study, AIHA was present in seven percent of cirrhotics. The significant correlation between the AHAI and the OAD, the HE and the advanced stage of the disease suggested the interest to evoke this diagnosis in front of a whole regenerative anemia.

Disclosure: Nothing to disclose

P0932

THE NEW PROFILE OF HDV-INFECTED PATIENTS IN SOUTHERN EUROPE

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Introduction: Delta hepatitis is a rare infectious disease caused by hepatitis delta virus (HDV). Since the Mediterranean basin is a traditional endemic region, we aimed to update in our area the epidemiological data on HDV infection and to confirm the greater aggressive nature of HDV-HBV coinfection compared to HBV mono-infection and describe risk factors for progressive disease.

Aims & Methods: Retrospective evaluation of anti-HDV-IgG seroprevalence among chronically infected HBV patients followed at a reference Hepatology Unit ($n=605$). Demographic, clinical, analytic, serologic and virologic parameters were retrieved from chart review together with evolution events (cirrhosis, liver decompensation, liver transplantation-LT, hepatocellular carcinoma-HCC and death). HDV-HBV patients were matched 1:1 by age and year of diagnosis to HBV mono-infected patients.

Results: 70 anti-HDV patients were included (11.5% of the HBV population) (table 1). Most (63%) were men and the median age was 52 years. Although most were born in Spain (67%), a non-negligible proportion (24.5%), particularly those more recently diagnosed, corresponded to immigrant population from Eastern European countries.

The profile of HDV-infected patients has substantially changed over the years, with a higher prevalence of Spanish-born, more frequently infected through intravenous drug use (IDU), and consequently more frequently coinfecting with either HIV or HCV among those diagnosed before the year 2000 and, in contrast, a significantly higher proportion of immigrants, presumably infected nosocomially in those diagnosed more recently.

Furthermore, comorbidities, such as diabetes (8.5%), obesity/overweight (55%) and alcohol consumption (34%) were frequent. Most (77%) progressed to cirrhosis. Liver decompensation (81%), HCC (16.5%) or LT (59.5%) were prevalent among cirrhotic patients.

Only one third of the sample (31.5%) had been treated with peg-IFN α therapy in the past. Diabetes was associated with progression to cirrhosis, LT and death. Male sex, increasing age and alcohol (or history of) consumption were associated with LT and HCC.

Compared to HBV mono-infected patients, delta-infected individuals developed more frequently cirrhosis and liver decompensation ($p < 0.000$), with no differences in HCC rates.

Conclusion: Patients diagnosed lately are frequently non-Spanish natives from endemic countries, in which iatrogenesis was presumably the infection route. Nevertheless, patients infected in the 80's through IDU are still a major concerning problem in our Unit given the aggressive nature of the

disease and frequent need of LT. Regardless of their origin, these are preferentially men with significant comorbidities, potentially playing a major role in disease progression.

Disclosure: Nothing to disclose

DEMOGRAPHIC AND SEROLOGIC PARAMETERS (%)		% (N)	Missing data (%)
Probable route of infection (%)	Unknown	45.7 (32)	0
	Iatrogenesis	20.9% (14)	
	Intravenous drug user	14.9% (10)	
	Other	26.4% (14)	
Diabetes Mellitus (%)	Diabetic	8.6% (6)	0
Alcohol consumption (%)	Alcoholic	34.3% (24)	1.4
HBe Antigen	HBeAg +	11.4% (8)	1.4
HIV	Anti - HIV +	10% (7)	5.7
HCV	Anti - HCV +	11.4% (8)	0
EVENTS (%)			
Cirrhosis progression		77.1% (54)	1.4
Liver decompensation		72.2% (39)	7.4
Liver cancer		12.9% (9)	0
Liver Transplant		45.7% (32)	0
Death (%)		5.7% (4)	0

[Table 1 - General characteristics (N=70)]

P0933

IMPACT OF HEPATITIS C VIRUS CLEARANCE BY DIRECT-ACTING ANTI-VIRALS ON RHEUMATOID ARTHRITIS DISEASE ACTIVITY

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Introduction: Patients with rheumatoid arthritis (RA) who are infected with hepatitis C virus (HCV) have been associated with higher pain and disease activity score (DAS28). In the past, interferon (IFN) based therapy for HCV was associated with low virologic response in addition to its potential to exacerbate RA activity and might even provoke RA in a number of reported cases. These concerns ended in suboptimal treatment of both diseases. Currently, direct-acting antiviral drugs (DAAs) are the standard of care for hepatitis C infection with high efficacy and safety.

Aims & Methods: **Aim:** To assess the impact of DAAs antiviral treatment of hepatitis C on rheumatoid arthritis disease activity. **Patients and methods:** Data of 638 patients with chronic hepatitis C infection who received DAAs were reviewed. Thirty-four patients with RA were included (26 with chronic hepatitis, 8 with cirrhosis). Clinico-laboratory evaluation including rheumatoid arthritis disease activity score-28 and sustained virologic response (SVR) were evaluated at baseline for DAS28 and 12-week post-treatment for both.

Results: **Results:** The SVR12 was achieved in 31 (91.2%) patients (100% for chronic hepatitis and 62.5% for cirrhosis). Only in patients with RA who achieved an SVR12 ($n = 31$), the mean value of DAS28 after HCV treatment was significantly lower than the baseline value (2.57 ± 0.59 vs. 4.71 ± 0.90 , $P < 0.001$, 95% CI: 1.81-2.49). Also, there was a significant decline in the mean values of serum anti-cyclic citrullinated peptide, rheumatoid fac-

tor, and erythrocyte sedimentation rate (ESR) after achieving an SVR12 (21.47±16.41 vs. 153.90±59.39 u/ml, 17.16±16.42 vs. 135.06±49.69 IU/ml, and 10.90±2.72 vs. 29.03±12.85 mm/h respectively; $P < 0.001$). There was a better disease control and better chance for step-down treatment after HCV treatment [51.6% with high activity, 38.7% with moderate activity, 6.5% with low activity, and 3.2% in remission before treatment vs. 0.0%, 12.9%, and 35.5% , and 51.6% with high, moderate, low, and remission state respectively, $P = 0.002$]. Baseline ESR, viral load, absence of cirrhosis, platelet count, alanine aminotransferase, and achieving an SVR12 were predictors of disease control in univariate analysis, while in multivariate analysis, baseline viral load and achieving an SVR12 were the only significant predictors of disease control ($P = 0.009$, and $P = 0.005$ respectively). No drug-related adverse events or drug-related discontinuation were reported.

Conclusion: Unlike interferon, HCV treatment by direct-acting antiviral drugs significantly improves rheumatoid arthritis disease control and treatment outcome with high safety and efficacy.

Disclosure: Nothing to disclose

P0934 WITHDRAWN

P0935 WITHDRAWN

P0936 WITHDRAWN

P0937

RISK OF HEPATITIS FLARE IN PATIENTS WITH PREVIOUS HEPATITIS B VIRUS EXPOSURE AMONGST PATIENTS ON BIOLOGICAL MODIFIER THERAPIES - RESULTS FROM A POPULATION-BASED STUDY

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Introduction: Biological modifier therapies are commonly used in the treatment of inflammatory bowel disease (IBD) and other auto-immune diseases and may cause hepatitis B virus (HBV) reactivation. Various new biological modifier therapies are now available. However, their exact risk of hepatitis B flare in patients with previous HBV exposure is poorly defined. We aimed to study the risk of hepatitis flare in patients on biological modifier therapies with previous HBV exposure.

Aims & Methods: All patients who were negative for HBsAg and received biological modifier therapies including anti-CD 20, anti-tumour necrosis factor (TNF), anti-cytokine therapies, anti-integrin, Janus Kinase (JAK) inhibitors and T cell or B cell activation blockers, from 1 January 2000 to 30 June 2019 were identified from a population-based database Clinical Data Analysis and Reporting System in Hong Kong. Patients who were positive for total antibody to hepatitis B core antigen (anti-HBc) and/or hepatitis B

surface antigen (anti-HBs) were defined to have previous HBV exposure. Patients were followed up until development of hepatitis flare, censored at the time of death, or the last ALT measurement at 5 years from the first dose of biological modifier therapy. Primary endpoint was development of hepatitis flare (alanine Aminotransferase [ALT] >80 IU/L).

Results: Total 2471 patients fulfilled the inclusion criteria (Anti-CD20 1284; Anti-TNF: 730; Anti-cytokine: 267; JAK inhibitors 121; T cell and B cell inhibitors 60; anti-integrin: 9). Median follow up duration was 28.3 months (Interquartile range: 8-60 months). Total 683 patients (27.6%) developed hepatitis flare. Cumulative incidence of hepatitis flare for patients receiving anti-CD20, anti-TNF, anti-cytokine, JAK inhibitors, T cell/B cell inhibitors and anti-integrin at 12 months were 27.3%, 10.8%, 13.3%, 8.2% and 9.7%, respectively. Cumulative incidence of hepatitis flare was significantly higher in patients on anti-CD20 ($p < 0.001$), but there were no significant differences in risks of hepatitis flare in patients receiving anti-TNF, anti-cytokine, JAK inhibitors, T cell/ B cell inhibitors and anti-integrins ($p = 0.82$). In multivariable analysis, use of prednisolone >40mg daily [adjusted hazard ratio (aHR) 1.46; 95% confidence interval (CI) 1.15-1.85], male gender (aHR 1.25; 95% CI 1.07-1.46), use of concomitant immunosuppressants (aHR 1.39; 95% CI 1.09-1.77) and lower albumin (aHR 1.04; 95% CI 1.03 -1.06) were risk factors for hepatitis flare after adjustment of baseline ALT level. Total 256 patients (10.4%) developed severe hepatitis flare (ALT > 200 IU/L). Cumulative incidence of severe hepatitis flare while on were anti-CD20, anti-TNF, anti-cytokine, JAK inhibitors, T cell/B cell inhibitors and anti-integrin at 12 months were 8.5%, 0.9%, 2%, 0.8% and 1%, respectively. Cumulative incidence of severe hepatitis flare was significantly higher in patients on anti-CD20 ($p < 0.001$), but there were no significant differences in risks of hepatitis flare in patients receiving anti-TNF, anti-cytokine, JAK inhibitors, T cell/ B cell inhibitors and anti-integrins ($p = 0.33$).

Conclusion: Amongst patients with previous HBV exposure who were treated with biological modifier therapies, 27.6% developed hepatitis flare. Cumulative incidences of hepatitis flare were similar in patients receiving anti-TNF, anti-cytokine, JAK inhibitors, T cell/B cell inhibitors and anti-integrin, ranging from 8.2%-13.3% at 12 months. Anti-viral prophylaxis should be considered in this group of patients.

Disclosure: Nothing to disclose

P0938 WITHDRAWN

P0939

NON-INVASIVE MARKERS FOR THE EXCLUSION OF ADVANCED FIBROSIS IN CHRONIC HEPATITIS C: EVALUATION OF APRI, FIB-4, GAMMA-GLUTAMYL TRANSFERASE TO PLATELET RATIO (GPR) AND RED CELL VOLUME DISTRIBUTION WIDTH TO PLATELET RATIO (RPR) COMPARED TO TRANSIENT ELASTOGRAPHY

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Introduction: Transient Elastography (TE) represents the most reliable non-invasive method to assess liver fibrosis. However, since TE is not widely available, there is an increasing need for simpler non-invasive markers. APRI, FIB-4, gamma-glutamyl transferase to platelet ratio (GPR) and red cell volume distribution width to platelet ratio (RPR) are simple laboratory markers that have been proposed as surrogate markers for TE.

Aims & Methods: Aim of our study was to evaluate the accuracy of these markers compared to TE regarding the assessment of liver fibrosis in chronic hepatitis C (CHC). We retrospectively analyzed 518 patients that underwent TE and laboratory tests between 2010 and 2018. We classified the results of TE that were >13 kPa as cirrhosis and >10k Pa as advanced fibrosis. Subsequently, we evaluated the APRI, FIB-4, GPR and RPR measurements with regards to the above classification.

Results: 158 (30.5%) patients were identified with advanced fibrosis and 108 (20.8%) with cirrhosis. The area under the curve for each marker is depicted in Table 1. APRI, FIB-4 and GPR show significantly better accuracy than RPR ($p < 0.001$ for all comparisons) for advanced fibrosis and APRI and FIB-4 show significantly better accuracy than RPR ($p = 0.02$ for both comparisons) for cirrhosis. By using the APRI 0.5, FIB-4 1.45 and GPR 0.6 cut-offs, we achieve 89.5%, 86.6% and 84.4% Negative Predictive Value (NPV) respectively, excluding advanced fibrosis in 39.6% 44.1% and 56.4% of patients, respectively.

Furthermore, using the APRI 1, FIB-4 1.45 and GPR 0.74 cut-offs, we achieve 88.5%, 92% and 89.3% NPV respectively, excluding cirrhosis in 64.1%, 46.8% and 65.4% of patients, respectively. Interestingly, the RPR 0.087 cut-off achieves 89.1% NPV, excluding cirrhosis in 70.9% of patients.

	APRI (n=518)	FIB-4 (n=518)	GPR (n=486)	RPR (n=399)
≥ F3	0.789	0.773	0.764	0.685
p-value	< 0.0001	< 0.0001	< 0.0001	< 0.0001
F4	0.811	0.791	0.761	0.727
p-value	< 0.0001	< 0.0001	< 0.0001	0.012

[Table 1. Area under the curve values for each marker, with regards to the stage of liver fibrosis, as assessed by transient elastography.]

Conclusion: APRI, FIB-4, GPR and RPR exhibit significant accuracy in assessing liver fibrosis in patients with CHC. The cut-offs proposed by international guidelines for APRI and FIB-4 are useful for the exclusion of advanced liver disease, while the GPR and RPR cut-offs introduced from our study may be used to further increase the number of patients excluded. These markers can be used as first-line tests, partially replacing TE, especially in areas where this is not available.

Disclosure: Nothing to disclose

P0940

NON-INVASIVE ASSESSMENT OF HEPATIC FIBROSIS IN CHRONIC HEPATITIS B: EVALUATION OF APRI, FIB-4, GAMMA-GLUTAMYL TRANSFERASE TO PLATELET RATIO (GPR) AND RED CELL VOLUME DISTRIBUTION WIDTH TO PLATELET RATIO (RPR) COMPARED TO TRANSIENT ELASTOGRAPHY

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Introduction: The assessment of liver fibrosis has a crucial role in the management of patients with chronic hepatitis B (CHB). Transient elastography (TE) is considered as the most accurate non-invasive method for evaluating hepatic fibrosis, but is not always available and its cost is high. Therefore, it is crucial to develop new non-invasive markers. Aspartate aminotransferase to platelet ratio index (APRI), Fibrosis-4 (FIB-4), gamma-

glutamyl transferase to platelet ratio (GPR) and red cell volume distribution width to platelet ratio (RPR) are simple markers that have been proposed to predict liver fibrosis.

Aims & Methods: Aim of this study was to evaluate the accuracy of these markers in the assessment of hepatic fibrosis, compared to TE, in patients with CHB. We retrospectively screened CHB patients who underwent TE between 2007 and 2018. They were hepatitis B antigen e (HBeAg) negative and received no treatment. Patients with TE > 11 kPa were classified as cirrhotics, according to recommendations of the American Gastroenterological Association. Then, we evaluated the diagnostic accuracy of APRI, FIB-4, GPR and RPR regarding the previous classification.

Results: 237 patients were screened. 25 (10.5%) patients were identified as cirrhotics. Area under the curve for APRI, FIB-4, GPR and RPR was 0.844, 0.844, 0.882, 0.837 respectively.

There was no significant difference between them. Using the cut-offs APRI 1 and FIB-4 1.45, we achieve 94.92% and 97.93% Negative Predictive Value (NPV), respectively, excluding cirrhosis in 90.78% and 66.82% of patients. Using APRI 2 and FIB-4 3.25, we achieve 92.79% and 93.63% NPV, respectively, excluding cirrhosis in 95.85% and 94% of patients.

The optimal cut-off of GPR is 0.45, achieving 86.36% sensitivity, 85.25% specificity and 98.1% NPV, excluding cirrhosis in 77.1% of patients. The optimal cut-off of RPR is 0.08, achieving 76.47% sensitivity, 87.61% specificity and 96.1% NPV, excluding cirrhosis in 75.38% of patients.

Conclusion: APRI, FIB-4, GPR and RPR present significant diagnostic accuracy compared to TE. The international recommended cut-offs of APRI and FIB-4 could exclude cirrhosis effectively. The optimal cut-offs of GPR and RPR proposed by our study could be useful for evaluating more adequately the stage of liver fibrosis. These markers may replace TE in the assessment of fibrosis in CHB patients, especially during the initial evaluation and in areas where TE is not available and affordable.

Disclosure: Nothing to disclose

P0941

VIROLOGIC RECURRENCE AFTER TREATMENT WITH DIRECT-ACTING ANTIVIRALS IN A COHORT OF PATIENTS WITH CHRONIC HEPATITIS C: PREDICTIVE FACTORS AND RETREATMENT EFFICACY

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Introduction: Direct-acting antivirals have revolutionized the treatment of chronic hepatitis C, and virologic recurrence is uncommon.

Aims & Methods: The aim of this study is to evaluate the predictive factors of virological relapse in a real-life cohort and the efficacy of retreatment in these patients.

An unicentric prospective cohort study, between February/2015 and February/2019, including patients with viral load determination at week 12 or 24 after treatment (treatment according to current guidelines), RVS per protocol - RVSP (excluding deaths and lost to follow-up) was analyzed. Statistical analysis performed with STATA, using the qui2 statistical test.

Results: There were 416 patients, 69% men, mean age 54 years (26-83), 31% cirrhotic (n = 130), 23 with decompensated cirrhosis (Child-Pugh-CP classification). Distribution by genotypes: G1: 65.1% (50.6%: 1b); G2: 1.7%; G3: 20.2%; G4: 12.5%; G5: 0.5%.

RVSP was 98.1% (408/416), with 8 relapses, all in cirrhotic patients (5 CP A and 3 CP B).

Recurrence was correlated with G3 ($p = 0.03$) and the presence of cirrhosis ($p < 0.001$): 100% RVSP (286/286) in the absence of cirrhosis, 95% in compensated cirrhosis (102/107) and 86.9% in decompensated cirrhosis (20/23). In the follow-up of the 8 relapsed patients, two died and 6 had a retreatment, 4 with RVS12 (see above) and one death due to hepatocellular carcinoma.

Age Genotype Treatment, weeks Retreatment, weeks

551asofosbuvir/ledipasvir,24sofosbuvir+elbasvir/grazoprevir+ribavirin,24
56 3 sofosbuvir/daclatasvir,24 sofosbuvir/velpatasvir/voxilaprevir,12

48 1 sofosbuvir/ledipasvir,24 sofosbuvir+elbasvir/grazoprevir+ribavirin,16
66 3 sofosbuvir/ledipasvir+ribavirin,24 sofosbuvir/daclatasvir+ribavirin,24

Conclusion: In this real-life cohort, virologic relapse was rare in relation to G3, stage of fibrosis and decompensated cirrhosis. In parallel, there is evidence of effective retreatment options for these patients.

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Disclosure: Nothing to disclose

P0942

ARE WE USING ULTRASONOGRAPHY APPROPRIATELY FOR THE SCREENING OF HEPATOCELLULAR CARCINOMA IN CHRONIC HEPATITIS B?: AN AUDIT OF CLINICAL PRACTICE IN SECONDARY CARE

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Introduction: Chronic hepatitis B (HB) is a known risk factor for hepatocellular carcinoma (HCC). At-risk patients should be screened using ultrasound scans (USS) every six months, but the indications differ between scientific bodies. This lack of agreement might lead to a misuse of resources. Our aim was to compare the performance of the current clinical practice guidelines in identifying at-risk patients in routine care [NNC1] and determine our adherence to such guidelines.

[NNC1] Por no repetir clinical practice en la misma frase.

Aims & Methods: An internal audit of our clinical practice was performed: we retrospectively reviewed the medical notes of HBsAg-positive patients and compared the number of follow-up USS performed between January 2015 and December 2018 against the EASL, AASLD and NICE guidelines' recommendations.

Results: 288 patients were included: 57% male, median age 45 years old (IQR 37 - 53). 74% were Caucasians, 7% African, 5% Asian and 9% from other ethnic backgrounds. 93% were HBeAg-negative. 2% had delta coinfection. 5% had family history of HCC. 17% did not undergo any USS during the selected time period. 14% had never been seen by a hepatologist. Using EASL guidelines, between 27% and 40% of patients fulfilled screening indication every semester. Among those with screening indication: 12 - 18% had six-monthly USS, 42 - 51% yearly USS and 31 - 45% did not have USS per studied year. Among those without screening indication: 2 - 6% had six-monthly USS, 27 - 38% yearly USS and 58 - 70% did not have USS per studied year. Differences between screening groups were statistically significant at every time point assessed ($p < 0.005$).

38% of patients did not undergo a transient elastography during the follow up period. There was no documentation of the ethnic background in 6% of the patients, nor of the family history of HCC in 37% of them. In 30% of the cases, delta serology was not available. These limitations made it difficult to accurately establish the screening indication as per the AASLD and NICE guidelines.

Screening indication could be positively established as per the AASLD and NICE guidelines in 11-13% and 9-13% patients/semester respectively. Of these, 12-25% and 9-27% had six-monthly USS, 37-57% and 43-57% yearly USS and 11-13% and 16-42% did not have USS per studied year, respectively.

Conclusion: The EASL guidelines allow for better identification of HCC at-risk patients who should undergo surveillance. According to them we underperformed between 94 and 130 USS/year and over performed between 70 and 90 USS/year during our study period. To improve adherence to current recommendations and to standardize clinical practice, we have protocolized HB follow up as per the EASL guidelines.

Disclosure: Nothing to disclose

P0943

FIVE YEAR FOLLOW UP AFTER TREATMENT WITH DIRECT ACTING ANTIVIRALS FOR HEPATITIS C: A SINGLE-CENTRE EXPERIENCE

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Introduction: Direct acting antivirals (DAAs) have revolutionised treatment of hepatitis C. However, their novelty means long-term outcome data is lacking. In particular, decompensated cirrhotics are an understudied group even in the pre-DAA era.

In 2014, NHS England approved the use of DAAs in a select group of patients in an Expanded Access Programme (EAP). Eligibility criteria included "significant risk of death or irreversible damage within the next 12 months". (1) These patients provide some of the longest follow up data after treatment with DAAs available to us, and in addition are an extremely sick cohort.

Aims & Methods: We retrospectively analysed the outcomes of 54 patients treated at a West London hospital through the NHS EAP between July 2014 and June 2015, mean follow up time of 51 weeks. Demographic, comorbidity and laboratory data were collected prior to treatment and at the latest clinical review.

Results: Response rate to treatment was 96%. Overall 1, 3 and 5 year survival was 92.6%, 85.2% and 75.9% respectively with a mean age at death of 58.8 years. A third of those still alive have had an episode of decompensation since starting treatment.

Significant predictors of mortality at 5 years include previous TIA/stroke, baseline MELD score 20-29 and baseline hyponatraemia. Significant predictors of survival include history of hypercholesterolemia, being Child Pugh A at baseline and having an initial MELD score <19.

Following treatment, there was a significant fall in ALT and AST, and a significant rise in albumin and all cholesterol markers. There was significant improvement in stiffness measured by transient elastography, with none having a stiffness <12kPa prior to treatment and 20% after. The percentage of patients with an APRI score <2.0 rose from 36.4% to 92%, and with a FIB-4 <3.25 (indicating fibrosis stage <4) rose from 6.8% to 25%.

The proportion of patients with clinically significant portal hypertension measured by the liver stiffness-spleen size-to-platelet ratio risk score fell from 91.3% to 88.5%. Prior to treatment, 4.3% met the Baveno IV criteria (for not requiring regular variceal surveillance), rising to 20.7% after treatment.

Total incidence of *de novo* HCC was 16.7%, with a mean annual rate of development 3.9% and a peak in the first 12 months (5.6%). Mean time between starting treatment and HCC being apparent on imaging was 26 months. 7 patients had an old HCC prior to treatment, 2 of whom had a recurrence at 22 and 40 months post treatment. Both had radiologically detectable lesion less than two months prior of starting treatment, but only diagnosed post treatment. The remaining 5 patients were all treated at least 11 months prior to DAA treatment.

Conclusion: Our data reflect some of the longest follow up in the sickest cohort of hepatitis C patients to date, and shows a clear regression of fibrosis and improvement in prognostic biomarkers, clinically significant outcomes and mortality scores in a significant proportion over a five year period. We identify a number of significant biomarkers for predicting increased mortality.

Further, while the risk of HCC is reduced with DAA treatment compared with no treatment in cirrhotics,⁽²⁾ there is an increased risk of *de novo* HCC in the first 12 months after treatment, and an increased risk of recurrence of HCC if treated less than 6 months after a radiologically apparent lesion is seen. These findings are significant for guiding the clinician on the appropriateness, timing and monitoring of DAA therapy in the sick cirrhotic cohort.

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Disclosure: Nothing to disclose

P0944

FIBROSIS REGRESSION AFTER HEPATITIS C TREATMENT: A RETROSPECTIVE COHORT STUDY

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Introduction: The emergence of direct-acting antivirals (DAAs) was a hallmark in Hepatitis C (HCV) treatment, since HCV eradication has been documented in most of the treated patients. Sustained virological response at 12 (SVR12) or at 24 (SVR24) weeks is the primary goal of HCV treatment, and it has been established that this achievement may regress hepatic fibrosis and, consequently, decreases the incidence of hepatic failure, portal hypertension complications and hepatocellular carcinoma. Liver fibrosis evaluation in HCV mono-infected patients by transient elastography (TE) has a confirmed diagnostic accuracy in several studies and meta-analyses.

Moreover, liver stiffness measurements (LSM) display a better prognostic value than histology for predicting liver related mortality and all-cause mortality in patients with hepatocellular carcinoma than biopsy, highlighting its use in HCV treated patients.

Aims & Methods: In this study, we aimed to evaluate fibrosis regression in patients who achieved SVR24, as well as to identify factors that influence fibrosis regression.

A single-centre, retrospective cohort study was conducted, with inclusion of all consecutive adult patients from the hepatology and infectious diseases consultations who achieved SVR24 after antiviral treatment against chronic HCV infection, between 2014 and 2019. Only patients with LSM by TE before and after the treatment were included. Patients with other causes of hepatic disease were excluded. The primary endpoint was fibro-

sis regression, defined as a 20% decrease in LSM after the treatment. Statistical analysis was performed using IMB statistical package for the social sciences (SPSS) version 25.

Results: 106 patients (76.4% male) were included in this study, with a median age of 53 years (IQR 45 to 60) at the date of HCV treatment initiation. The median difference between pre-treatment and post-treatment LSM was 2.0 kPa (IQR -0.1 to 4.7) ($p < 0.001$). Overall, 58.9% of patients achieved fibrosis regression after treatment. In patients with a pre-treatment fibrosis stage higher than F3, fibrosis regression achievement was more frequent (33.9% of F0-F2 patients vs 64.8% of F3-F4 patients, $p < 0.01$). The median time between the end of treatment (EOT) and post-treatment LSM was higher in patients who achieved fibrosis regression [60.5 weeks (36.5 to 86.8)], when compared with patients who did not achieve this endpoint [34 weeks (21 to 59.5)] ($p < 0.01$).

No significant relationship was found between fibrosis regression and gender ($p = 0.904$), age ($p = 0.987$), different antiviral regimens ($p = 0.454$) and the use of ribavirin ($p = 0.214$).

Conclusion: Effective antiviral treatment against HCV chronic infection resulted in an overall decrease in LSM in this patients.

Fibrosis regression was more frequent in patients with a more advanced pre-treatment fibrosis stage.

In the group of patients who achieved fibrosis regression, the median time between the EOT and post-treatment LSM by TE was higher, when compared with the group patients who did not achieve this endpoint.

Disclosure: Nothing to disclose

P0945

CLINICAL CHARACTERISTICS OF PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND HEPATITIS B VIRUS (HBV) INFECTION

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Introduction: Hepatitis B virus (HBV) infection is considered to be associated with lower risk of non-alcoholic fatty liver disease (NAFLD) if there is not a concurrent metabolic disorder.

Aims & Methods: The aim of this study is to assess the clinical and laboratory characteristics of patients with NAFLD and HBV infection (NAFLD-HBV). The medical charts of NAFLD patients referred to outpatients' clinic due to abnormal liver biochemistry and/or the presence of fatty liver were thoroughly reviewed.

Results: The medical charts of 569 NAFLD patients were initially retrieved; Sixty-eight patients were excluded because of other chronic liver diseases. Finally, 501 patients were included in the study (M/F: 266/235), 388 NAFLD (M/F: 199/189) and 113 NAFLD-HBV patients (M/F: 67/46). NAFLD-HBV patients had significantly higher levels of γ GT ($p = 0.030$), ALP ($p = 0.036$) and INR ($p = 0.030$) compared to NAFLD patients. Moreover, a significantly lower percentage of NAFLD-HBV patients were overweight or obese compared to pure NAFLD patients ($p = 0.007$) and the presence of HBV infection was correlated with lower risk of obesity or overweight (RR: 0.876).

Conclusion: Patients with NAFLD and HBV comorbidity exhibited more impaired liver function tests compared to NAFLD patients. Furthermore, HBV infection was associated with reduced probability of increased body-weight.

Disclosure: Nothing to disclose

P0946

MICROELIMINATION OF HEPATITIS C IN PATIENTS WITH CHRONIC HEMOLYTIC ANEMIAS: A SINGLE CENTER EXPERIENCE

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Introduction: Patients with chronic haemolytic anemias (CHA) are at a high risk for transfusion-transmitted infections. Various studies in Egypt have shown a prevalence of hepatitis C virus (HCV) infection in 24% - 37% of those patients who are also more likely to develop cirrhosis at a young age. Elimination of HCV in patients with CHA would prevent early progression of liver disease.

Aims & Methods: In this study we aimed to assess the efficacy, safety, and tolerability of sofosbuvir (SOF) and daclatasvir (DAC) in HCV-infected patients with CHA. 21 consenting hepatitis C patients (median age: 33, range: 18-62 years, males: 9 [42.9%], females: 12 [57.1%], Child-Pugh score A [52.3%], B [47.7%]) with different types of CHA (12 beta-thalassemia major, 5 intermedia, 1 minor, 1 sickle cell anemia, 1 sickle thalassemia, and 1 cryoglobulinemia) were recruited and treated at Ain Shams University viral hepatitis treatment and research center using ribavirin-free SOF/DAC regimen for either 12 or 24 weeks according to categorization of patients into easy or hard-to-treat in accordance with the national protocols. Sustained virological response was assessed by RT-PCR for HCV-RNA at 12 weeks post-treatment (SVR12). Any treatment-related adverse events were noted. None of the patients showed sonographic features of liver cirrhosis or hepatic focal lesions.

Results: All patients were adherent to treatment with no discontinuation of therapy. SVR12 was achieved in 19 out of 21 patients (90.5%). Two non-responder beta-thalassemia major patients were found to be on regular blood transfusion before and during treatment, in addition to increased transfusion requirements after treatment which makes them at high risk for a possible re-infection. There was a significant difference between levels of total bilirubin and ALT ($p < 0.024$ and $p < 0.001$, respectively). On the other hand, hemoglobin and ferritin levels showed a non-significant difference ($p < 0.991$ and $p < 0.6$, respectively). Assessment of changes in blood transfusion requirements showed no change in 15 patients (71.4%), a decrease in a single patient (4.8%), and an increase in 5 patients (23.8%). Moderate adverse events were observed in 2 out of 21 patients (9.5%), including sickling crisis and drop in hemoglobin level; none though necessitated discontinuation of treatment.

Conclusion: The results of this study substantiate the favourable efficacy, safety, and tolerability of ribavirin-free DAAs in the special population of HCV-infected patients with CHA. Treatment is recommended early in the course of infection to eliminate the virus, prevent horizontal transmission, and avert relentless progression of liver disease.

Disclosure: Nothing to disclose

P0947

SAFETY AND PREGNANCY OUTCOME OF ANTI-HCV DIRECT-ACTING ANTIVIRALS: REAL-LIFE DATA FROM AN EGYPTIAN COHORT

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Introduction: Considerable percentage of chronic hepatitis C patients are females in childbearing period. None of the direct-acting antivirals (DAAs) for chronic hepatitis C is currently approved for use in pregnant females. Data on the safety and pregnancy outcome of DAAs in pregnancy are still lacking.

Aims & Methods: We aimed to study safety of DAAs and pregnancy outcomes in a series of women who get pregnant during chronic HCV treatment. This study included data of patients treated in centers of the Egyptian National Committee for Control of Viral Hepatitis. We retrieved the data of the first 100 consecutive female patients with chronic hepatitis who had negative serum pregnancy test prior to the first dose of DAAs and discovered to be pregnant during on-treatment follow-up visits. All patients were evaluated by a hepatologist and obstetrician at discovery of pregnancy. All patients were advised to stop DAAs and to have regular follow-up visits in viral hepatitis treatment center and obstetrics clinic till delivery. Regular follow-up visits included detailed history for any adverse events, thorough clinical examination, complete blood counts, kidney and liver tests, in addition to prenatal care visits at obstetrics clinic. Anomaly scan was scheduled at 18-20 weeks of pregnancy.

Results: Our study included 100 chronic hepatitis C patients with a mean age of 30 ± 6.7 years. Only 3 (3%) patients had comorbidities, they had diabetes and hypertension. All patients (100%) were treatment-naïve and had HCV mono infection, and one patient (1%) had liver cirrhosis (Child-Pugh class A). All patients received 12-week anti-HCV treatment regimens which included: sofosbuvir plus daclatasvir (SOF/DCV) in 95 patients (95%), SOF/DCV plus ribavirin (RBV) in 3 patients and paritaprevir/ritonavir/ombitasvir plus RBV in 2 patients. Sixty-two patients (62%) denied the use of any contraceptive methods, 19 used barrier contraception (male condom), 15 used oral contraceptive pills, 2 used intrauterine contraceptive devices and 2 used injectable hormonal contraceptives. Ninety-one patients (91%) stopped DAAs (at on-treatment weeks 4-8), while 9 completed a full course of DAAs despite of medical advice to stop treatment. Out of the studied 100 pregnant ladies, 58 (58%) had delivered normal babies, 18 expect normal babies (based on anomaly scan) and 22 had missed follow-up. Out of the 58 babies, 51 (87.9%) were born full term and

7 (12.1%) early term. Two patients had postpartum hemorrhage and one neonate developed physiological jaundice. No major adverse events related to DAAs, liver decompensation, renal impairment, fetal anomalies, or maternal, fetal or neonatal mortalities were reported. Out of the 9 patients who completed the full course of DAAs, 5 (55.5%) patients delivered normal babies, two are still pregnant and two were lost to follow-up. Only 5 (5%) patients attended their post-treatment week 12 visit and all (100%) achieved sustained virological response.

Conclusion: In our cohort of pregnant females, anti-HCV DAAs were safe without fetal anomalies or related adverse pregnancy outcomes.

Disclosure: Nothing to disclose

P0948

CHRONIC VIRAL HEPATITIS IN A COHORT OF INFLAMMATORY BOWEL DISEASE PATIENTS: A CASE-CONTROL STUDY

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Introduction: We aimed to perform an epidemiologic study to assess the prevalence of chronic viral hepatitis in inflammatory bowel disease (IBD) and to detect the possible relationships between the two conditions.

Aims & Methods: In a single center cohort cross-sectional study, consecutive IBD patients and controls were recruited. All patients underwent laboratory investigations to detect chronic hepatitis B (HBV) and hepatitis C (HCV) infection. Parameters of liver function, liver elastography and features of IBD were collected. Univariate analysis of factors associated to chronic viral hepatitis was performed by Student's t or chi-square test. Multivariate analysis was performed by binomial logistic regression. For independent variables odds ratios (OR) were calculated.

Results: We enrolled 807 subjects with IBD; 35 (4.3%) had chronic viral hepatitis, in particular 28 HCV (3.5% versus 5.3% in controls, $p=0.24$) and 7 HBV (0.9% versus 0.5% in controls, $p=0.64$). A serology indicative of HBV vaccination was observed in 232 (28.7%) patients and vaccinated patients were younger than non vaccinated ones (43.1 ± 14.1 versus 45.9 ± 16.2 years, $p=0.02$). Previous contact with hepatitis B virus, landmarked by HBc IgG positivity and HBV DNA negativity, was found in 62 patients (7.7%). Patients with chronic viral hepatitis had a higher mean age and lower frequency of smoking and alcohol consumption. These subjects showed higher frequency of diabetes, hypertension and wider waist circumference. They suffered more frequently from ulcerative colitis. Instead, CD patients with chronic hepatitis had undergone less surgical operations; in detail, the 50% (4 out of 8) of patients with surgical procedures performed before 1990 had HCV, while patients undergoing surgery after 1990 did not show any type of viral hepatitis ($p < 0.001$). Liver stiffness was greater in subjects with chronic viral hepatitis than in those without this condition (7.0 ± 4.4 versus 5.0 ± 1.2 KPa; $p < 0.001$). At multivariate analysis, only the age directly correlated with the risk of viral hepatitis (OR=1.05, 95% CI 1.02-1.08, $p < 0.001$).

Conclusion: Despite the endemic presence of both viruses, the prevalence of HBV/HCV in IBD is low in our geographic area. Age may be the only independent factor of viral hepatitis-IBD association. Possible explanation may be HBV vaccination and HCV detection and prevention in younger patients.

Disclosure: Nothing to disclose

P0949

LONG TERM IMPACT OF HCV ERADICATION ON DYNAMICS OF LIVER FIBROSIS

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Introduction: Liver fibrosis is the natural end result of chronic HCV infection and is responsible for almost all liver related complications. Recently there was a big advance in therapeutics of HCV with marvelous rates of viral clearance. Liver fibrosis would expectedly improve when the underlying etiology is eliminated. Many studies showed significant improvement of liver fibrosis shortly after successful HCV cure however tracing of liver fibrosis thereafter and possibility of cirrhosis reversal have been scarcely addressed in the literature.

Aims & Methods: We aimed to trace dynamical changes in liver fibrosis 1, 3 and 5 years after HCV eradication.

Methods: Six hundred and fifty five chronic HCV patients who received direct acting antiviral agents (DAAs) and successfully cured have been prospectively followed up for changes in liver fibrosis through serial measurement of liver stiffness (LSM) at 1, 3 and 5 years after HCV cure.

Results: The mean age was 51.44 ± 10 years, 73% of patients were males. 52% of patients had no cirrhosis; while the rest were cirrhotics.

In non cirrhotics, the mean baseline LSM was 8.29 ± 2.3 kPa that was significantly declined to 4.03 ± 1.0 kPa at 5th year ($p < 0.001$). In cirrhotics, the mean baseline LSM was 29.66 ± 14.25 kPa that was significantly declined to 22.50 ± 11.16 kPa at 5th year ($p < 0.001$).

There was a significant down shifting of LSM concordant to F2 and F3 at the baseline to that concordant to F0-1 at all time points of follow up yet more evident at 1st year and reached the maximum proportion at the 5th year; F0-1, F2, F3 was 17.7%, 17.9% and 16.6% at baseline and became 56.5%, 4.1% and 4.9% at 5th year respectively.

On the other hand, cirrhosis had regressed to lower stages of fibrosis in 87 patients (27.7%); patients labeled as F4 were 313 at baseline and became 226 at 5th year.

The overall mean changes in LSM were -1.67 ± 0.93 , -0.74 ± 0.44 and -0.61 ± 0.55 kPa at 1, 3 and 5 years respectively with higher declines in cirrhotics than non cirrhotics; -2.5 ± 0.52 , -1 ± 0.36 and -1.1 ± 0.32 versus -0.96 ± 0.57 , -0.51 ± 0.50 and -0.17 ± 0.40 kPa respectively.

Conclusion: There was a significant regression of advanced liver fibrosis and a substantial reversal of liver cirrhosis on long term after sustained HCV eradication while mild stages of fibrosis can be vanished at earlier time.

Disclosure: Nothing to disclose

P0950

THE ROLE OF DIABETES MELLITUS IN THE DEVELOPMENT OF HEPATOCELLULAR CARCINOMA IN HEPATITIS C VIRUS-INFECTED PATIENTS TREATED WITH DIRECT-ACTING ANTIVIRALS: A META-ANALYSIS

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Introduction: Hepatitis C virus (HCV)-infected patients treated with direct-acting antivirals (DAAs) are still at risk of developing hepatocellular carcinoma (HCC) after sustained virologic response (SVR). Therefore, it is important to find predictive factors for HCC development in this population.

Higher rates of comorbidities, particularly diabetes was highlighted to favor carcinogenesis and might be associated with the incidence of HCC in the DAA treated SVR group.

Aims & Methods: This study aimed to investigate the role of diabetes mellitus (DM), as a potential predictive risk factor, in the development of HCC in HCV-infected patients after DAA treatment.

This study was registered on PROSPERO under registration number CRD42020176781. We performed a systematic search in three medical databases.

Studies were eligible if they reported on HCV-infected patients with SVR who had at least one year of follow-up after DAA treatment, and reported the frequency of incident and/or recurrent HCC in patients with and without DM. We calculated pooled hazard ratios (HR) with 95% confidence intervals (CIs) in meta-analysis.

Results: Fourteen cohort studies were included. DM proved to be a significant risk factor of HCC in HCV patients in univariate analysis (HR=1.52, CI=1.18-1.95), which association was less prominent but significant after adjustment for covariates (HR=1.29, CI=1.01-1.63). In the subgroup of liver cirrhosis, the point estimate was similar but non-significant (HR=1.54, CI=0.91-2.62). Besides, DM was not a significant predictor of HCC recurrence (HR=1.27, CI=0.79-2.05).

Conclusion: DM seems to be an independent risk factor of developing HCC after DAA treatment in HCV-infected patients; therefore, we suggest a more rigorous follow-up in this group.

Disclosure: Nothing to disclose

P0951

VIRAL HEPATITIS B REACTIVATION UNDER BIOLOGICAL THERAPY: SCREENING AND PREVENTION MODALITIES IN RHEUMATIC AND INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Viral hepatitis B reactivation (VHBr) is a serious complication of immunomodulatory therapy and in particular biological therapy (BT), which can be life threatening, whence the adoption by societies of screening and prevention strategies based on the risk of VHBr which depends on serological status and the treatment used.

Aims & Methods: The objective of our study was to determine the modalities of HBV screening, to describe the prevalence of HBV infection in this group of patients, and to evaluate the VHBr prevention strategies adopted in our country.

This was a retrospective, 8-year [2011-2018], single-centre, descriptive, retrospective study conducted in two departments: Rheumatology and Hepato-Gastroenterology. Patients under BT were included. Records with missing data were excluded. The modalities of screening and prevention of VHBr were determined and the prevalence of HBV markers was investigated.

Results: One hundred patients were included: 85 followed up for chronic inflammatory rheumatic disease: rheumatoid arthritis (n=40), ankylosing spondylitis (n=41), juvenile idiopathic arthritis (n=4) and 15 patients followed up for inflammatory bowel disease (11 Crohn's disease and 4 ulcerative colitis). The mean age was 44 years with a predominance of females (59%). The BTs prescribed were anti-TNF α , anti-IL6 and antiCD20 in 83%, 11% and 7% respectively.

HBV screening was done in 89% of cases: HBsAg was tested in 89%, anti-HBc in 64% and anti-HBs in 43%. Complete B serology (HBsAg, anti-HBc and anti-HBs) was performed in 40%.

One patient had chronic hepatitis B on Entecavir for 3 years before starting anti-CD20 (HBsAg(+), anti-HBc(+)). A previous contact with HBV as evidenced by isolated anti-HBs(+) positivity was noted in 13 patients (20%). A negative B serology was noted in 30 patients (30%). The vaccination rate was 10%.

Prophylaxis with Entecavir was indicated in 2 patients at high risk of viral B reactivation (candidates for anti-CD20 therapy and having anti-HBc(+) with undetectable viral load). One patient at moderate risk of reactivation (candidate for anti-TNF therapy and having anti-HBc(+)) was placed on Lamivudine for prophylaxis. Pre-emptive therapy based on monitoring of alanine aminotransferase (ALT) and HBV DNA levels every 1 to 3 months was indicated in 10 patients (with anti-HBc (+) and candidates for BT other than anti-CD20) but correctly applied in only 2 patients (20%). The remaining eight patients were monitored only for ALT levels. No cases of viral reactivation B were objectified.

Conclusion: In our study, viral hepatitis B screening was done correctly in 40% of the cases. The rate of VHB vaccination was low (10%) despite the low cost of the vaccine. Prophylactic and pre-emptive treatment for viral reactivation were correctly applied in 100 and 20% of cases respectively. This underlines the difficulties encountered in applying pre-emptive treatment when access to HBV DNA level determination is limited and warrants more vigilance prior to the prescription of BT.

Disclosure: Nothing to disclose

P0952

ELIMINATION OF HEPATITIS C VIRUS INFECTION AMONG PWUIDS AS PART OF THE NATIONAL EGYPTIAN MACROELIMINATION TEST AND TREAT PROGRAM

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Introduction: Illicit drug users are the core of the persistent hepatitis C virus (HCV) epidemic in Western countries. However, Egypt is experiencing a surge in illicit drug use reaching twice the global rates amid combating the long-standing HCV epidemic through its national test and treat campaign. **Aims & Methods:** We aimed to characterize the profile of HCV-infected persons who used drugs (PWUDs) and study the outcome of sofosbuvir-based regimens in this marginalised population in Egypt.

In the current study, among 9580 HCV- infected patients, presenting to the viral hepatitis treatment unit at Ain Shams university hospitals (Faculty of Medicine Ain shams Research Institute (MASRI), 300 were PWUIDs between January 2016 - March 2019. Only 234 patients completed their treatment (12 weeks) according to the national guideline protocol. These patients were recruited from addiction specialized centres where they received their treatment and follow-up as part of the governmental mass treatment program without discriminated from other patients to avoid being stigmatized. Patients were treated with different sofosbuvir-based regimens (SOF/DAC; SOF/DAC/RBV; PAR/OMB/RBV; SOF/SIM).

Treatment response was determined by sustained virological response (SVR) 12 weeks after the end of treatment. Adverse events were monitored during treatment.

Results: Patients' median age was 44 years old. Most of the patients were males (96.6%); while 35 (14.9 %) were multiple drug users. The illicit drugs used in order of frequency were: cannabis, heroin, tramadol, alcohol, and benzodiazepines. three patients were cirrhotic at baseline. Eight patients were HIV co-infected and one patient was HBV co-infected.

SVR was achieved in 202 (86.3%) patients. There was no significant association between SVR and type of drug substance used. While, there was significant association between SVR and treatment type; where SVR was high among those treated by SOF/SIM (100%), followed by SOF/DAC (90.6%), SOF/DAC/RBV (83.5%), and the least was PAR/OMB/RBV (68.0%). Non-response (13.7%) could be related to many factors including non-compliance of patients ; 43.8% of non-responders were using cannabis while 31.3% were heroin users. Anemia was detected only in 4 patients.

Conclusion: A relatively high efficacy and safety to sofosbuvir-based treatment regimens among HCV infected PWUDs, when compared with non-drug users. Studies on the best choice of HCV treatment combination regimen for Egyptian PWUDs are essential to inform a targeted coverage of PWUDs, which is an urgently needed policy to eliminate HCV infections among this key population and its importance to reduce social and economic harm to individuals and society.

Disclosure: Nothing to disclose

P0953

NONINVASIVE ASSESSMENT OF LIVER FIBROSIS - COMPARING ACOUSTIC RADIATION FORCE IMPULSE ELASTOGRAPHY WITH SERUM MARKERS

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Introduction: Liver fibrosis evaluation is essential for predicting prognosis and defining treatment strategies and follow-up of hepatitis C virus (HCV) infected patients. Liver biopsy remains the gold-standard in liver fibrosis assessment. However, its limitations led to the development of noninvasive new approaches.

Aims & Methods: Our main purpose was to evaluate the concordance between liver acoustic radiation force impulse (ARFI) elastography and serum markers for liver fibrosis evaluation in chronic hepatitis C. We performed a retrospective study including HCV infected patients with ARFI elastography between 2015 and 2019. Elastography was performed using Siemens Acuson S2000 ultrasound system and the results were compared with concurrent results from serum markers: AST to Platelet Ratio Index (APRI), Fibrosis-4 (Fib-4), AST-ALT Ratio (AAR), King's Score e Fibrosis Index. Cutoff values for determining liver fibrosis using ARFI were F_{≥2}: 1.34 m/s; F_{≥3}: 1.55 m/s; F₄: 1.80 m/s.

Results: Two hundred and eighty-seven patients were included, with a mean age of 49 years old, 72.9% were male. The most frequent genotype was G1 (74.5%), followed by G3 (15.7%), G4 (8%) and G2 (1.8%). On ARFI elastography, median shear wave speed was 1.41m/s (IQR 1.23-2.00) with 40.3% of patients presenting values compatible with F0/1, 20.5% with F_{≥2}, 10.4% with F_{≥3} and 28.8% with F4. There was a statistic significant, moderate and positive correlation between ARFI elastography and serum markers: APRI (rs=0.56; p< 0.001), Fib-4 (rs=0.53; p< 0.001), King's Score (rs=0.59; p< 0.001) and Fibrosis Index (rs=0.50; p< 0.001). The concordance level for cirrhosis or advanced fibrosis between ARFI and serum markers was: moderate with APRI (K=0.54; p< 0.001), Fib-4 (K=0.45; p< 0.001) and King's score (K=0.42; p< 0.001) and low with AAR (K=0.14; p=0.02) and Fibrosis Index (K=0.27; p< 0.001).

Conclusion: There was a significant and moderate correlation on the assessment of liver fibrosis between ARFI elastography and serum markers. The concordance between ARFI and APRI, Fib-4 and King's score in fibrosis evaluation reaffirms its use in clinical practice as useful indicators of the degree of liver fibrosis.

References: J Hepatol 2015; 63: 237-264 J Viral Hepat. 2012 Feb;19(2):e212-9; World J Gastroenterol. 2006 Jun 21;12(23):3682-94; J Hepatol. 2013 Mar;58(3):593-608; Hepatology. 2011 Mar;53(3):726-36.

Disclosure: Nothing to disclose

P0954

ROLE OF DIRECT ANTIVIRAL TREATMENTS IN THE EVOLUTION OF VIRAL CIRRHOSIS C

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Introduction: Direct antiviral (DAT) treatments have made the eradication of Hepatitis C virus infection (HCV) possible in 90% of cases in cirrhotic patients.

Aims & Methods: The aim of our work was to reassess the contribution of these treatments on the evolution cirrhosis.

This is a retrospective study collecting patients followed for viral cirrhosis C having had antiviral treatment (DAT) (Sofosbuvir / Ledipasvir +/- Ribavirin) between 2016 and 2019. Patients with follow-up of less than 3 months have been excluded. The characteristics of cirrhosis before and after treatment were analyzed.

Results: During this period, we included 89 active viral cirrhosis C. Seventy-eight patients had genotype 1b, 5 patients had genotype 2 and only one patient had genotype 4. These were 20 men and 69 women. The average age was 67 years [35-85 years]. Eighteen percent had diabetes and 20% had high blood pressure. Child-Pugh score was A, B and C in 63%, 29% and 5% of cases, respectively. Before treatment with DAT, 27% had presented at least an episode of ascites decompensation, 14% an episode of gastrointestinal bleeding, 5% an episode of hepatic encephalopathy, 3% an episode of spontaneous bacterial peritonitis and 11% a hepatocellular carcinoma candidate for curative treatment. Sixty-one percent of patients were DAT-naïve. Patients treated previously with dual therapy : PEGylated interferon and Ribavirin were non-responders in 40% of cases and relapsers in 40% of cases. Sofosbuvir / Ledipasvir were prescribed alone or in combination with ribavirin in 72% and 27% of patients, respectively. The sustained virological response rate (SVR) was 98%. The mean follow-up was 24 months [6-36 months]. After treatment, the rate of complications was: 2% of gastrointestinal bleeding, 22% of ascites decompensation and absence of encephalopathy and spontaneous bacterial peritonitis ($p < (10^{-4})$). Eight cases (9%) of hepatocellular carcinoma were detected after SVR.

Conclusion: In our series, the SVR rate in patients with viral cirrhosis C was 98% and was associated with a significant decrease in complications except for hepatocellular carcinoma.

Disclosure: Nothing to disclose

P0955

ADVANCED CHRONIC LIVER DISEASE AFTER DIRECT-ACTING ANTIVIRAL TREATMENT FOR HEPATITIS C

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Introduction: Direct-acting antiviral (DAA) treatment for hepatitis C was revolutionary, mainly due to its high efficacy and safety, even in patients with advanced liver disease. However, more data on the long term morbidity due to hepatic disease in this group of patients submitted to this treatment is required.

Aims & Methods: We performed a retrospective study including patients with advanced hepatic fibrosis due to Hepatitis C virus (HCV) treated with DAA from February 2015 to December 2018. Our main purpose was to evaluate morbimortality after treatment. Liver fibrosis was evaluated with acoustic radiation force impulse technology (ARFI) using Siemens Acuson S2000 ultrasound system.

Results: One hundred and three patients were included in this study, 78.6% were male with a mean age of 52.96 (± 10.17) years. HCV genotype 1 was the most prevalent (78.8%). 74.8% of patients presented stage 4 fibrosis and the remaining stage 3 with a median ARFI shear wave speed of 2.30 m/s (IQR 1.79-2.81). 90.2% of patients presented Child-Pugh A, 6.9% were Child-Pugh B and 2.9% were Child-Pugh C, with a mean MELD score of 9 (IQR 7-12). The mean time of follow-up was 37 (± 14) months after treat-

ment. Sustained virologic response at 12 weeks was achieved in 97.1% of patients. Median shear wave speed reduced to 1.71m/s (IQR 1.37-2.29) ($p < 0.001$) and MELD score to 8 (IQR 7-10) ($p < 0.017$). A statistically significant difference in Child-Pugh classification was not obtained ($p = 0.102$). Five patients developed hepatocellular carcinoma (incidence rate of 1.5/100 per year): all were male, mean age was 56.6 (± 3.0) years, 20% were Child-Pugh A, 60% Child-Pugh B and 20% Child-Pugh C. Four patients died being only two deaths related with hepatic disease (one due to hepatocellular carcinoma).

Conclusion: The use of DAA showed a high cure rate in hepatitis C patients with advanced liver fibrosis as described in Literature. A reduction in hepatic fibrosis evaluated by ARFI was reported as well as an improvement in liver function assessment (MELD score). The incidence and mortality rate of hepatocellular carcinoma in this study was similar to other series and may justify long-term surveillance.

References: J Viral Hepat. 2012 Feb;19(2):e212-9; Mini Rev Med Chem. 2018;18(7):584-596

Disclosure: Nothing to disclose

P0956

HEPATITIS B REACTIVATION DURING HEPATITIS C TREATMENT

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Introduction: HBsAg-positive individuals were excluded from clinical trials of direct-acting antivirals (DAA). The alert to the risk of reactivation of hepatitis B virus (HBV) during hepatitis C virus (HCV) treatment was emitted after DAA came into clinical use. In patients HBsAg negative and anti-HBc positive the risk of reactivation appears to be very low.

Aims & Methods: To assess the risk of HBV reactivation during the treatment of Hepatitis C

Retrospective study that included all patients with previous contact with HBV who underwent HCV treatment in our hospital from 2012 to 2018.

Results: A total of 110 patients were identified, 79% were male ($n = 87$), with a mean age of 50 ± 8 years 107 HBc Ab positive HBsAg negative and 3 HBsAg positive, 56% were positive for anti-HBs Ab (46/82). The HCV treatments used were Ledipasvir / Sofosbuvir (51%), Elbasvir / Grazoprevir (14%), Velpastavir / Sofosbuvir (6%), Glecaprevir / Pibrentasvir (6%), others (23%). The median duration of therapy was 12 [8-24]weeks. All except 2 patients had sustained virological response.

None of the patients HBsAg negative and anti-HBc positive had HBV reactivation.

Of the 3 HBsAg positive patients, there was HBV reactivation in 2; these patients were HBeAg negative, HIV negative, HDV negative, with elevated ALT and DNA-HBV levels. One of the cases had detectable viral load (244 IU / mL). After the institution of entecavir, both had suppression of HBV viral load.

Conclusion: Our results suggest that HCV patients with HBsAg negative and anti-HBc positive serology are a safe population to treat with DAA, with no apparent risk of HBV reactivation.

In HBsAg positive patients, the alert for the use of concomitant prophylactic HBV therapy is reinforced, since 2 in 3 had reactivation.

Disclosure: Nothing to disclose

P0957

SARCOPENIA IN CHILDREN AND YOUNG ADULTS WITH PRIMARY SCLEROSING CHOLANGITIS AND IBD

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Introduction: Malnutrition is common in children with inflammatory bowel disease (IBD) and in liver diseases. The nutritional status can be assessed by evaluating for sarcopenia, which is described as the loss of muscle mass and/or strength that are reflected by decreased psoas muscle surface area (PMSA). Accumulating data shows association of PSMA with chronic diseases, however, literature regarding sarcopenia in children is still limited. The aim of this study is to assess sarcopenia in children and young adults with sclerosing cholangitis (PSC) with or without IBD.

Aims & Methods: Retrospective analysis of patients below 25 years of age diagnosed with PSC between the years 2010-2018 was done. Patients who performed magnetic resonance imaging (MRI) were included in the study. Detailed clinical, anthropometric, laboratory and imaging findings were recorded. The control group was comprised of children who underwent MRI due to suspected scoliosis or kidney structural anomalies and had normal study. PMSA was determined at intervertebral disc L3.

Results: Sixty five patients were included in the study. Twenty with PSC with mean age of 15.2±5 years, 12 were female and 9 had IBD. The control group comprised of 45 healthy subjects with no significant difference in age, gender and BMI from the study group. There was no significant difference in PMSA between groups. However, PMSA significantly correlated with aspartate transaminase (AST) and Platelet Ratio Index (APRI) score (marker for hepatic fibrosis, $r=-0.49$, $p=0.02$). Additionally, PMSA was significantly higher in patients who had both PSC and IBD (475.61±136 vs. 789±328, $p=0.01$).

Conclusion: Children and young adults with concomitant PSC and IBD were in a better nutritional status in comparison to patients with PSC alone, as evidenced by lesser degree of sarcopenia. Additionally, sarcopenia correlates to the degree of liver fibrosis assessed by APRI score. Further larger studies are warranted in order to corroborate the importance of sarcopenia in patients with PSC.

Disclosure: Nothing to disclose

P0958

IDENTIFICATION & SERVICE EVALUATION/IMPROVEMENT OF A PRIMARY SCLEROSING CHOLANGITIS COHORT USING NATURAL LANGUAGE PROCESSING

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Introduction: Recent BSG guidelines¹ make recommendations about the management of patients with primary sclerosing cholangitis (PSC). PSC is, however, a rare condition with no UK unique ICD-10 diagnostic code. This adds to the challenge of retrospective case identification and thorough service evaluation, thus why we chose to use a novel natural language processing (NLP) methodology.

Aims & Methods: Records from all patients with PSC at our hospital between 2008-2020 were identified using our NLP methodology involving fuzzy matching and tokenizing related texts for analysis. Anonymised discharge summaries, clinic letters, radiology reports, endoscopy records and histology, were digitally-trawled in order to identify the cohort characteristics. Patients with inconclusive radiology/biopsy were excluded.

Results: We identified 500 patients with 'potential' PSC. Patients with diagnostic uncertainty, IgG4 disease or secondary causes were removed, leaving 234 with a further 93 excluded as either deceased or followed up elsewhere. 16 patients received a liver transplant and were excluded from service evaluation, leaving 125 patients.

39.2%(49) of these 125 cases were missed during a parallel manual audit. Given our hospital serves a tertiary population of around 1,900,000², this suggests a point prevalence of 6.95 per 100,000; 20% higher than typically cited UK figures³. 59.2% had concurrent IBD (Table 1). Introduction of a joint PSC/IBD clinic in December 2018 achieved a 25% reduction of 2019 clinic activity.

Subgroup	Mean Total GI Clinic Rate / Year	Gastroenterology Mean Clinic Rate / Year	Hepatology Mean Clinic Rate / Year	Mean USS/MRCP rate / Year	Mean Colonoscopy rate / Year
PSC+IBD (n=74)	2.51(+/-0.23)	1.27(+/-0.22)	1.24(+/-0.24)	0.82(+/-0.11)	0.49(+/-0.18)
PSC Only (n=51)	2.26(+/-0.29)	0.07(+/-0.07)	1.99(+/-0.38)	0.83(+/-0.11)	0.07(+/-0.04)
T-test	(p=0.38)	(p=0.002)	(p=0.002)	(p=0.96)	(p<0.001)

[Table 1: Subgroup service characteristics with 95% confidence intervals]

Conclusion: PSC cohorts are difficult to identify due to a lack of a UK clinical code. An NLP based method proved highly effective at identifying all cases within our institution, with a 64.5% increase compared to conventional methods. The analysis showed that historic outpatient clinic rates were high while surveillance investigation rates were not in keeping with new guidelines. Introduction of a combined PSC/IBD clinic as a targeted service delivery intervention is addressing this shortfall with an already significant impact after 1 year.

References: 1. Chapman MH. Gut. 2019 Aug 1;68(8):1356-78. 2. Inspection Report. CQC 2019. 3. Liang H. Medicine (Baltimore). 2017;96(24): e7116.

Disclosure: Nothing to disclose

P0959 WITHDRAWN

P0960

AUTOIMMUNE LIVER DISEASES RISE RISK FOR ACCELERATED ATHEROSCLEROSIS: A PILOT STUDY

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Introduction: According to the known data, chronic inflammation can increase arterial stiffness and is associated with accelerated atherosclerosis.

Aims & Methods: Our aim was to determine if it is plausible for autoimmune liver diseases. Values of both arterial stiffness markers, augmentation index (AIx) and pulse wave velocity (PWV), were measured in patients

with autoimmune liver diseases, as well as other possible risk factors for increased arterial stiffness, as marker of atherosclerotic changes and higher cardiovascular risk in patients with autoimmune liver diseases. We have enrolled 38 patients (3 male, 35 female; average age 58.7 ± 9.6) diagnosed with autoimmune liver disease (4 patients with autoimmune hepatitis, 24 patients with primary biliary cholangitis and 10 patients with primary sclerosing cholangitis) from UHC Zagreb. Blood pressure was measured three times (Omron M6) and mean values were calculated. Arterial stiffness markers; PWV and Alx were measured by Arteriograph and mean values were calculated. The assessment of liver stiffness/fibrosis was determined with transient elastography (FibroScan), and steatosis grade with CAP (controlled attenuation parameter). Fasting blood and 24-hour urine samples were collected. Sodium and potassium were determined using Kawasaki equation. There were 8.4% of patients with prior diabetes and 5.2% of patients with prior hypertension, respectively.

Results: Mean PWV was 9.7 m/s which is above cut-off values for pathological large artery stiffness while mean Alx was also increased (32.8%). Arterial stiffness was increased in 42.1% of patients. There were 42.1% of patients with diagnosed hypertension, while 18.7% of them were on prior antihypertensive therapy. PWV was positively correlated with age, sedimentation rate,

c-reactive protein and central systolic blood pressure while negatively with glomerular filtration rate. Alx was positively correlated with heart rate and central systolic blood pressure while interestingly not with age. Linear regression analysis showed positive association of duration of disease, sedimentation rate, total cholesterol and triglycerides and liver stiffness with increased Alx while increased PWV was positively associated with age, duration of disease, sedimentation rate, total cholesterol and triglycerides, and liver steatosis grade. When we have compared patients with $PWV < 9$ m/s we have found that patients with $PWV > 9$ m/s were significantly older, had higher sedimentation rates, lower GFR, higher total cholesterol, LDL cholesterol, systolic and diastolic blood pressure and central systolic blood pressure values as well as higher steatosis grade. When we compared patients with different chronic autoimmune liver diseases we have not found significant differences.

Conclusion: Patients with chronic autoimmune liver diseases have increased arterial stiffness markers in comparison to general population which confirms our hypothesis that chronic inflammation has impact on increased arterial stiffness. Duration of disease, presence of dyslipidemia and chronic inflammation, liver steatosis and fibrosis grade, together with traditional risk factors like age, contributes to increased risk for future cardiovascular events. This could implicate that screening for arterial hypertension and increased arterial stiffness should be a part of workup algorithm in patients with autoimmune liver diseases, especially if there are signs of liver steatosis, in order to determine risk for future cardiovascular events. Further investigation, on larger patients cohorts are needed.

Disclosure: Nothing to disclose

P0961

TACROLIMUS AND THE COMBINATION WITH OTHER IMMUNOSUPPRESSIVE AGENTS IS AN EFFECTIVE THERAPEUTIC APPROACH FOR IGG4-RELATED DISEASE

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Introduction: IgG4-related disease (IgG4-RD) is considered as a systemic, chronic inflammatory syndrome, characterized by enlargement of involved organs, elevated levels of IgG4, dense lymphoplasmocytic infil-

trates, rich in IgG4-positive plasma cells, and fibrosis in involved organs. The optimal treatment has not been established yet. As an initial treatment, glucocorticoids are recommended. In patients with relapse along with glucocorticoid dose reduction, various immunosuppressive agents have been reported. Azathioprine, mycophenolate mofetil (MMF), rituximab, and calcineurin inhibitors (CNI) are the most frequently used drugs in these refractory cases. Here we report the effectiveness of tacrolimus and the combination with other immunosuppressive drugs in patients with IgG4-RD.

Aims & Methods: We reviewed patients with IgG4-RD in our institution and identified 5 patients with relapse, who were treated with tacrolimus or with the combination of tacrolimus and other immunosuppressive agents or targeted immunomodulators (everolimus, methotrexate, and rituximab).

Results: The first patient is a 75-year-old Caucasian male diagnosed with an IgG4-positive cholangitis, relapsing after initial use of steroids and treatment with azathioprine and later on with purinethol. After treatment with tacrolimus, liver enzymes and IgG4 rapidly normalized and bile duct dilatations disappeared. The second patient is a 57-year-old man, also diagnosed with an IgG4-positive cholangitis with highly elevated serum IgG4-levels.

After treatment with steroids and azathioprine, the patient with secondary biliary cirrhosis underwent successfully liver transplantation. No elevated serum IgG4 concentrations were detected after transplantation under immunosuppressive therapy with tacrolimus and everolimus. As the third patient, we report a 61-year old man with IgG4-related fibro-inflammatory condition in multiple organs and high IgG4-levels. Because of a severe case of psoriasis, the patient was treated with methotrexate. IgG4-related autoimmune pancreatitis, lymphadenitis, and sialadenitis were effectively treated with tacrolimus in combination with methotrexate. Serum IgG4-levels decreased immediately and clinical improvement was reported. As the fourth patient, we demonstrate a 34-year old man with IgG4-related autoimmune hepatitis and lymphadenitis. The patient with elevated IgG4-serum level suffered from relapse after treatment with steroids, azathioprine, and MMF.

After treatment with tacrolimus in combination with rituximab, a significant decrease of IgG4-level was detected and liver enzymes normalized. The fifth patient is a 63-year old woman, initially diagnosed with ulcerative colitis with overlap to PSC. Later the diagnosis of IgG4-positive cholangitis was determined after surgical removal of the gallbladder. In this case, treatment with steroids was not sufficient and azathioprine was not tolerated. A normalized IgG4-level was detected with a combined treatment of tacrolimus and rituximab.

Conclusion: IgG4-RD generally responds to glucocorticoids in its inflammatory stage, but recurrent or refractory cases are common. Other immunosuppressive agents and targeted immunomodulators are appealing to overcome potential side effects of glucocorticoids. Here we demonstrate that tacrolimus, especially in combination with other immunosuppressive agents and targeted immunomodulators, is a reasonable alternative in patients with steroid-dependent and thiopurine-refractory IgG4-RD.

Disclosure: Nothing to disclose

P0962

RISK OF DEVELOPING PRIMARY BILIARY CHOLANGITIS IN PATIENTS WITH ISOLATED POSITIVE ANTI-MITOCHONDRIAL (AMA) ANTIBODIES

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Introduction: The presence of AMA is highly specific (95%) for the diagnosis of primary biliary cholangitis (PBC) in patients with abnormal alkaline phosphatase. The presence of AMA without any other signs of PBC has also been described but the data regarding its relevance and the risk of developing PBC in these patients is scarce. The aims of the study were: 1) to evaluate the prevalence of AMA positivity in our centre, and 2) to assess the incidence and risk factors of developing PBC in patients with normal liver tests and positive AMA.

Aims & Methods: Retrospective analysis of all patients who underwent AMA testing in a single center between 2006 and 2010. AMA were analyzed by indirect immunofluorescence on rat liver/kidney/stomach slides. Patients were divided in 3 groups: previous PBC diagnosis (under treatment and followed at the outpatient hepatology clinic), *de novo* PBC diagnosis (AMA positivity, high AP and/or compatible histology) and patients without PBC (AMA positivity without other PBC criteria).

Results: During the study period 35,740 AMA testing in 19,431 patients were performed, 1069 were positive corresponding to 468 patients (2.4%). Most of the positive patients were women (n=406, 86%) with a median age of 59 years (47-69) and a prevalence of autoimmune comorbidity of 35% (n=164). In 69% (n=322) of cases, the test was requested because of liver tests abnormalities, in 18% (n=84) to study systemic diseases, and in the remaining 12% (n=64) due to other reasons. Two-hundred thirty-two patients (50%) had a previous diagnosis of PBC and 59 (19%) were new diagnosis. A hundred and seventy-seven (38%) had positive AMA with no other criteria of PBC. Most of these patients were women (n=142, 80%), with a median of 55 years (44-71). Seventy-seven patients (43%) had other autoimmune comorbidities, being Sjögren syndrome (n=29) and systemic lupus erythematosus (n=17) the most frequent. Sixteen patients (9%) developed PBC after a median follow-up of 8 years. These patients were more frequently women (100% vs. 77%, p=0.020) with autoimmune comorbidities (75% vs 43%, p=0.013). There were not significant differences in the titers of ANA, AMA, anti-M2, or anti-gastric parietal cell antibodies, the pattern of ANA, and the levels of alkaline phosphatase. Ten out of the 10 patients who developed PBC had a liver stiffness measurement at the time of diagnosis with a median value of 5.2 kPa (range: 4.1-35.8).

Conclusion: The prevalence of AMA positivity in our centre is low. A non-negligible proportion of AMA positive patients do not fulfill PBC criteria. Nine percent of AMA positive patients developed PBC during follow-up. Therefore, due to the progressive nature of the disease, a clinical and analytical follow-up of these patients is mandatory.

Disclosure: Nothing to disclose

P0963

A TREATMENT TO CONSIDER: MULTIVISCERAL TRANSPLANTATION FOR PORTO-MESENTERIC VENOUS THROMBOSIS

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Introduction: Intestinal (IT) and Multivisceral transplantation (MVT, transplantation of the stomach, small bowel, pancreas and liver) are established treatments for patients with complications of intestinal failure, and large benign abdominal tumours necessitating evisceration.

More recently, porto-mesenteric venous thrombosis (PMVT), with or without underlying liver disease, has become an emerging indication for MVT [1]. Isolated liver transplantation in these patients is either technically impossible, or unable to treat the complications of portal hypertension. MVT is therefore indicated in a select group of patients to replace the porto-mesenteric system.

Aims & Methods: As one of the largest European centres in IT and MVT, we present a case series of patients with PMVT who underwent transplantation at Addenbrooke's Hospital, Cambridge, UK.

A retrospective review of all patients who underwent IT or MVT between 2007 and March 2020. Data is collected prospectively in a local database, which was interrogated to identify all patients in whom porto-mesenteric vein thrombosis was the primary indication, with or without liver disease. Where appropriate, UKELD and MELD scores were calculated at closest time point before transplantation.

Results: 105 intestinal and multivisceral transplants in 98 patients were performed in total for the last 13 years. Transplantation for PMVT were first performed in 2011, and 23 have been done to date, accounting for 23% of IT and MVT since 2011.

Of these, 8 patients had no underlying liver disease, 14 patients had clinical, histological and radiological evidence of cirrhosis or advanced fibrosis from a variety of aetiologies. 1 remaining patient had nodular regenerative hyperplasia of the liver.

Out of the patients with PMVT without liver disease, 3 patients had concurrent Budd-Chiari Syndrome. Umbilical vein sepsis of infancy was suspected or confirmed in 4 patients, and 2 patients had underlying thrombophilia.

13 (57%) of the procedures were MVT, and 7 (30%) were liver-pancreas-intestine transplants, which are increasingly performed in recent years. Furthermore, whilst majority of patients received liver containing grafts, 3 patients with non-cirrhotic PMVT underwent isolated IT. 2 were performed to reduce portal pressure by allowing systemic drainage of the transplant intestine, as a treatment for refractory and complicated portal hypertension, and the third allowed for en-bloc removal of a high grade ampullary tumour in the context of extensive PMVT, where a Whipple's procedure was contraindicated.

1- and 5-year survival rates were 86% and 46%, respectively. Notwithstanding small number of patients at long term follow up, the 5-year survival is comparable in liver-pancreas-intestine transplant patients (2/3) and MVT patients (4/10), and in patients with liver disease (5/10) and those without liver disease (1/3).

Conclusion: Intestinal and multivisceral transplantation is a viable treatment for a select group of patients with diffuse PMVT. Technical advances include preservation of the native stomach, spleen and pancreaticoduod-

denal complex where possible and pre-operative embolization of the mesenteric arteries to reduce intra-operative blood loss. Suitable patients should be considered for early referral and assessment in a multidisciplinary setting, involving hepatology, liver and multivisceral transplant teams.

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Disclosure: Nothing to disclose

P0964

NONINVASIVE ASSESSMENT OF GRAFT STEATOSIS AND FIBROSIS AFTER LIVER TRANSPLANTATION BY TRANSIENT ELASTOGRAPHY

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Introduction: By increasing number of liver transplant recipients and improvement of liver transplant outcomes, non-invasive surveillance of graft steatosis and fibrosis is increasingly needed. Transient elastography (TE) is now widely used and accepted for diagnosis and assessment of patients with chronic liver disease of various etiologies. However, data about usefulness of TE in post-transplant period is very limited.

Aims & Methods: This study aimed to investigate steatosis and fibrosis of liver allograft by TE and its usefulness for prediction of mortality in liver transplant recipients. Between July 2017 and October 2017, all adult liver transplant recipients referred to our outpatient liver transplant clinic were included. We included patients who passed 6 months of liver transplant surgery in Shiraz Transplant Center. Transient elastography (TE) was performed measuring both controlled attenuation parameter (CAP) and liver stiffness by one experienced hepatologist based on standard methods. Clinical and laboratory data of patients were recorded. Patients were followed for a period of 2 years after TE for the main outcome of mortality. Univariate and multivariate Cox regression method and logistic regression model were used for statistical analysis. Statistical analysis was performed Using SPSS software.

Results: A total of 296 liver transplant recipients were included. There were 175 men and 121 women with a mean age of 42.51 ± 13.28 years. Sixty nine patients (23.3 %) fulfilled criteria for metabolic syndrome after liver transplantation. Hepatitis B virus (HBV) was the most common cause of underlying liver disease in our patients. The mean time from liver transplant to TE assessment was 36.39 ± 32.77 months. In Cox regression analysis, non-alcoholic steatohepatitis (NASH) as the main etiology of liver cirrhosis (OR=3.61, 95 % CI: 1.70 - 7.63; P-value= 0.001) and post-transplant diabetes mellitus (PTDM) (OR=3.11, 95 % CI: 1.09- 8.84; P-value= 0.033) were independent predictor of hepatic steatosis after liver transplantation diagnosed by TE. Seventy three patients (24.7 %) had different degrees of liver fibrosis in TE. Thirty one patients (10.5 %) had F1, 27 patients (9.1 %) had F2, 6 patients (2 %) had F3 and 8 patients (2.7 %) had F4 liver fibrosis. Using Cox regression model, alanine aminotransferase (ALT) (OR=1.01, 95 % CI: 1.00- 1.02; P-value= 0.019) was associated with liver fibrosis in TE. Mortality was occurred in 12 patients during 2 years follow-up. In logistic

regression analysis, presence of liver fibrosis as assessed by TE was an independent predictor for mortality of liver transplant recipients in a 2 years follow-up (OR=5.06, 95 % CI: 1.02- 25.04; P-value= 0.047).

Conclusion: Steatosis and fibrosis of liver allograft are prevalent in long term liver transplant recipients as assessed by TE. TE might be considered for follow-up of patients and might predict mortality in this group of patients.

	Odds ratio	95 % CI	P-value
Age	0.999	0.97-1.02	0.945
Etiology of liver disease	3.61	1.70 -7.63	0.001
Body mass index	0.889	0.58-1.35	0.586
PTDM	3.11	1.09- 8.84	0.033
Hyperlipidemia	0.818	0.39-1.71	0.594
Hypertension	0.897	0.46-1.72	0.745
Rejection	0.829	0.40-1.71	0.613
Waist circumference	0.964	0.92-1.08	0.964
Hip circumference	1.03	0.95-1.11	0.423

[Cox regression analysis of risk factor for allograft steatosis after liver transplantation]

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Disclosure: Nothing to disclose

P0965

PRE-TRANSPLANT SARCOPENIC OBESITY WORSENS THE SURVIVAL AFTER LIVER TRANSPLANTATION: A META-ANALYSIS AND A SYSTEMATIC REVIEW

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Introduction: Rising prevalence of cirrhotic cases related to non-alcoholic steatohepatitis has led to an increased number of cirrhotic patients with the coexistence of obesity and muscle mass loss called as sarcopenic obesity (SO). In patients undergoing liver transplantation (LT), the presence of SO may worsen prognosis and increase morbidity and mortality.

Aims & Methods: We aimed to evaluate the effect of the presence of pre-transplant SO on the outcomes of LT. A comprehensive search was performed in seven medical databases for studies comparing morbidity and mortality of patient with SO to patients without SO (non-SO) after LT. The primary outcome was overall mortality on short- (1 year), intermediate- (3 years), and long-term (5 years). Pooled relative risks (RRs) with 95% confidence intervals (CIs) were calculated. Heterogeneity was quantified with I²-statistics.

Results: Based on the analysis of 1,515 patients from three articles, SO increased overall mortality compared to non-SO at short-, intermediate-, and long-term follow-up (RR=2.06, 95% CI: 1.28-3.33; RR=1.67, 95% CI: 1.10-2.51; and RR=2.08, 95% CI: 1.10-3.93, respectively) without significant between-study heterogeneity for short- and intermediate-term (I²=0.0% for both) and considerable heterogeneity for long-term follow-up (I²=81.1%).

Conclusion: Pre-transplant SO proved to be a risk factor after LT and associated with two times higher mortality at short and long-term follow-up. Since SO worsen the prognosis of patients after LT, inclusion of body composition assessment before LT may help to plan a more individualised nutritional treatment, physiotherapy, and postoperative care and may improve morbidity and mortality.

Disclosure: Nothing to disclose

P0966

IMPACT OF LIVER SUPPORT SYSTEMS IN ACUTE-ON-CHRONIC LIVER FAILURE: UNCERTAINTY REMAINS - A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: The role of artificial and bioartificial liver support systems in acute-on-chronic liver failure (ACLF) is still controversial. Several extracorporeal techniques have been tested in randomized controlled trials and further analyzed in pairwise meta-analyses.

Aims & Methods: Our aim was to perform the first network meta-analysis comparing different liver support systems to each other and to standard medical therapy (SMT) in patients with ACLF. A Bayesian network meta-analysis of randomized controlled trials was conducted. The systematic search was performed on December 15, 2019 in 5 databases (MEDLINE, EMBASE, CENTRAL, Web of Science and Scopus) without any restrictions or filters.

Data extraction was performed by two independent investigators (KO, AK) in duplicate and in case of discrepancies agreement was reached by the help of an expert. Data on overall (OS) and transplant-free (TFS) survival, hepatic encephalopathy, laboratory parameters (including bilirubin, ammonia, creatinine) and adverse events were collected. Heterogeneity was tested by χ^2 test and I^2 test. For ranking the interventions, we chose to use the surface under the cumulative ranking (SUCRA) curve. To check for publication bias, a visual inspection of funnel plots will be performed with Egger's test. The RoB2 tool and grade approach were used for risk of bias (ROB) assessment and quality of evidence (QE) was assessed using the GRADE approach.

Results: The systematic search yielded 2797 results. 23 trials were eligible for inclusion. 16 trials were included in the quantitative synthesis, enrolling 1606 patients, using MARS®, Prometheus®, ELAD®, plasma exchange (PE) and BioLogicDT®. 1- and 3-month OS and TFS were assessed quantitatively. PE significantly improved 3-month OS compared to SMT (RR 0.74, CI: 0.6-0.94) and ranked first on the cumulative ranking curves in 3 outcomes. ELAD® only suggested survival benefit at 1-month TFS, ranking first before PE. Regarding other comparisons, MARS® seemed to perform better than ELAD®, Prometheus®, BioLogicDT® and SMT, but it did not reach statistical significance. Laboratory parameters, adverse events and hepatic encephalopathy (HE) were included in the qualitative synthesis. All studies reported improvement of HE, although not always significant. MARS®, Prometheus®, PE and ELAD® reduce bilirubin levels, whilst BioLogic-DT® was found to be ineffective in this regard.

All studies proved to be safe, but some treatment-related adverse events were also reported. Less than half of the studies had low risk of bias and QE in general was of low or very low grade.

Conclusion: Available extracorporeal liver support therapies are effective in reducing bilirubin levels and they might improve survival and hepatic encephalopathy. Plasma exchange seemed to be the most beneficial regarding survival, but better designed studies are needed to come to firm conclusions in the future.

Disclosure: Nothing to disclose

P0967 WITHDRAWN

P0968

HIGH FRAME-RATE CONTRAST ENHANCED ULTRASOUND (HIFR-CEUS) IN THE CHARACTERIZATION OF SMALL HEPATIC LESIONS IN CIRRHOTIC PATIENTS

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Introduction: To show the effectiveness of HighFrame-Rate CEUS (HiFR-CEUS) compared with conventional CEUS (C-CEUS) in the characterization of small (< 2 cm) focal liver lesions (FLLs) not easily detected by CT in cirrhotic patients. C-CEUS is limited by the transmission principle, and its frame-rate is around 10 FPS. With HiFR-CEUS, the frame-rate reached 170 FPS.

Aims & Methods: Ultrasound detected small FLLs (< 2 cm) in 63 cirrhotic patients during follow-up (June 2019-February 2020); (7 nodules < 1 cm and were not evaluable by spiral CT). Final diagnosis was obtained with MRI (47) or fine needle aspiration (16 cases).

C-CEUS was performed and HiFR-CEUS was repeated after 5 minutes; 0.8-1.2 ml of contrast media (SonoVue, Bracco, Italy) was used. 57 nodules were better evaluable with HiFR-CEUS; 6 nodules were equally evaluable by both techniques; final diagnosis was: 44 benign lesions (29 hemangiomas, 1 amartoma, 2 hepatic cysts; 2 focal nodular hyperplasias, 3 regenerative macronodules, 3 AV-shunts, 3 hepatic sparing areas and 1 focal steatosis) and 19 malignant one (17 HCCs, 1 cholangiocarcinoma, 1 metastasis); statistical evaluation for better diagnosis with χ^2 test (SPSS vers. 26); we used LI-RADS classification for evaluating sensitivity, specificity PPV, NPV and diagnostic accuracy of C- and HFR-CEUS. Corresponding AU-ROC were calculated.

Results: C-CEUS and HiFR-CEUS reached the same diagnosis in 29 nodules (13 nodules >1< 1,5 cm; 16 nodules >1,5< 2 cm); HiFR-CEUS reached a correct diagnosis in 32 nodules where C-CEUS was not diagnostic (6 nodules < 1 cm; 17 nodules >1< 1,5 cm; 9 nodules >1,5< 2 cm); C-CEUS was better in 2 nodules (1 < 1 cm and 1 >1< 1,5 cm). Some patient's (sex, BMI, age) and nodule's characteristics (liver segment, type of diagnosis, nodule's dimensions ($p=0,65$)) were not correlated with better diagnosis (p ns); only better visualization ($p=0,004$) was correlated;

C-CEUS obtained the following LI-RADS: type-1: 18 Nodules, type-2: 21; type-3: 7, type-4: 7; type-5: 8; type-M: 2; HiFR-CEUS: type-1: 38 Nodules, type-2: 2; type-3: 4, type-4: 2; type-5: 15; type-M: 2;

In comparison with final diagnosis: C-CEUS: TP: 17; TN: 39; FP: 5; FN: 2; HiFR-CEUS: TP: 18; TN: 41; FP: 3; FN: 1;

C-CEUS: sens: 89,5%; Spec: 88,6%; PPV: 77,3%; NPV: 9,5,1%; Diagn Acc: 88,6% (AU-ROC: 0,994± SE_{AUC}: 0,127; CI: 0,969-1,019); HiHFR CEUS: sens: 94,7%; Spec: 93,2%; PPV: 85,7%; NPV: 97,6%; Diagn Acc: 93,2% (AU-ROC: 0,9958± SE_{AUC}: 0,106; CI: 0,975-1,017).

Conclusion: Both C-CEUS and HiFR-CEUS are good non invasive imaging system for the characterization of small lesions detected during follow up of cirrhotic patients.

HiFR-CEUS allowed better FLL characterization in cirrhotic patients with better temporal and spatial resolution capturing the perfusion details that cannot be easily observed with C-CEUS.

Disclosure: Nothing to disclose

P0969

DIAGNOSTIC PERFORMANCE OF TWO-DIMENSIONAL SHEAR WAVE ELASTOGRAPHY WITH PROPAGATION MAPS ANALYSIS FOR QUANTIFICATION OF LIVER FIBROSIS AND STEATOSIS

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Introduction: New 2DSWE method with propagation maps analysis has been recently introduced by Cannon. It may be used for liver stiffness measurement (LSM), coupled by dispersion analysis, assessment of liver viscoelastic properties, and attenuation imaging (ATI) for assessment of steatosis. Only limited evidence exists for their clinical applicability.

Aims & Methods: We aimed to test diagnostic performance of the new 2DSWE method for liver fibrosis and steatosis assessment. We prospectively included healthy participants and patients with chronic liver diseases of different etiologies. All participants underwent LSM and ATI (5 measurements) by Applio i800 ultrasound (US) system. Transient elastography (TE) served as the reference method for both LSM (8 kPa for F_≥2, 10 kPa for advanced fibrosis (F_≥3)/compensated advanced chronic liver disease (cACLD) and 15 kPa for cirrhosis (F=4), according to Baveno VI recommendations) and steatosis assessment (controlled attenuation parameter (CAP) 248 dB/m for S_≥1, 268 dB/m for S_≥2 and 280 dB/m for S3). LSM by TE and 2DSWE were considered reliable when IQR/median was < 30%.

Results: Final cohort of 170 patients with paired LSM was created with median age (IQR) and BMI (IQR) of 60 (46-67) years and 28.0 (24.0-31.0) kg/m², respectively; 88 (51.8%) males. Total of 59 (34.7%) patients had significant fibrosis (F_≥2), 45 (26.5%) had advanced fibrosis/cACLD, while 26 (15.3%) had cirrhosis. Pearson correlation between TE and 2DSWE was r=0.76 for fibrosis and r=0.53 for steatosis assessment. Optimal (Youden) 2DSWE cut-off values were 6.55 kPa for F_≥2 (AUROC 0.878), 7.15 kPa for F_≥3 (AUROC 0.911) and 8.8 kPa for cirrhosis (AUROC 0.970). Optimal ATI cut-off (N=152) for S1 steatosis (N=95) was 0.625 dB/cm/MHz (AUROC 0.77), for S2 (N=80) 0.715 dB/cm/MHz (AUROC 0.77) and for S3 (N=67) 0.745 dB/cm/MHz (AUROC 0.734). LSM of 7.95 kPa by 2DSWE had 93.26% NPV for ruling-out cACLD, whereas 19.8 kPa had 91.61% PPV to ruling-in cirrhosis. In the group of healthy volunteers (N=31) mean value of 2DSWE LSM was 4.84 kPa (95% CI 4.35-5.32) ranging from 2.5 to 9.2 kPa.

Conclusion: New 2DSWE with propagation maps analysis is reliable method for noninvasive assessment of chronic liver disease. It has better diagnostic performance for fibrosis staging than for quantification of liver steatosis.

Disclosure: Nothing to disclose

P0970

WHICH IS BETTER FOR THE NONINVASIVE ASSESSMENT OF LIVER FIBROSIS? POINT OR TWO-DIMENSIONAL SHEAR WAVE ELASTOGRAPHY?

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Introduction: Ultrasound based elastography is a family of ultrasound-based imaging techniques that can measure liver stiffness (LS), quantifying mechanical properties of tissues, and has exhibited potential in detecting, grading, and monitoring progression of liver fibrosis in patients, replacing liver biopsy in several scenarios.

Aims & Methods: The goal of this study was to compare the noninvasive diagnostic performance of two elastography techniques for the diagnosis of liver fibrosis, in a cohort of patients with known hepatitis C virus, using Transient Elastography as the reference method.

The study included 176 patients, all with chronic hepatitis C, mean age 60.7 ± 9.0 years, mean body mass index (BMI) 26.9 ± 4.4 kg/m², the majority being women 69.1% (105/152). Liver stiffness (LS) was evaluated during the same session by means of three elastography methods: point Shear Wave Elastography (pSWE) using ElastPQ technique (EPIQ 7 ultrasound system, Phillips), Two-Dimensional Shear Wave Elastography (2D-SWE) from GE (LOGIQ E9 ultrasound system, General Electric) and Transient Elastography (TE; FibroScan, EchoSens).

Liver stiffness measurements (LSMs) were considered failures when no value was obtained after 10 attempts. Reliable LSMs were defined, for all techniques, as the median value of 10 valid measurements with an interquartile range/median (IQR/MED) < 30%. For the prediction of significant fibrosis (F_≥2), advanced fibrosis (F_≥3) and cirrhosis (F=4), we used the following cut-off values: 7.0, 9.5 and 12 kPa(1). The diagnostic performance of 2D-SWE.GE and ElastPQ for staging liver fibrosis compared to TE (reference standard) was estimated using the area under the receiver operating characteristics (AUROC) curves analysis and comparisons were made between both methods using TE as reference.

Results: Valid LSMs were obtained in 93.1% (164/176) of patients using 2D-SWE.GE, 92.6% (163/176) using ElastPQ and 95.4% (168/176) using TE. There was no significant difference between the feasibility rates of TE, ElastPQ, and 2D-SWE.GE (p=0.507). A good correlation was found between the liver stiffness (LS) values obtained using the two elastographic methods (r=0.78). The mean LS values obtained using the ElastPQ technique were significantly higher than those obtained using 2D-SWE.GE (12.1±7.3 kPa versus. 10.4±4.0 kPa, p< 0.0001). Pairwise comparisons of ROC curves between 2D-SWE.GE and ElastPQ have shown that there are no significant differences in their performance for staging F_≥2 fibrosis (p=0.89), F_≥3 fibrosis (p=0.76), and F=4 fibrosis (p=0.86).

Conclusion: We found that both methods exert excellent feasibility and diagnostic performance for the non-invasive assessment of liver fibrosis with similar performance for staging significant, advanced fibrosis, and liver cirrhosis.

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Disclosure: Nothing to disclose

P0971

DIAGNOSTIC ACCURACY OF DIFFERENT MODALITIES IN CYSTIC FIBROSIS-RELATED LIVER DISEASE: A DIAGNOSTIC ACCURACY NETWORK META-ANALYSIS

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Introduction: Pancreato-hepato-biliary complications are one of the leading causes of morbidity and mortality in cystic fibrosis (CF). European guidelines recommend annual screening for liver involvement which are hard to determine objectively.

Therefore, other non-invasive diagnostic methods (ultrasound-based techniques and fibrosis scores) were proposed to be alternative screening tools for CFLD.

Aims & Methods: A Bayesian diagnostic test accuracy network meta-analysis to rank the performance of the new non-invasive diagnostic methods was performed on studies about CF patients who underwent different diagnostic tests (index tests) and the components of the Debray and Colombo criteria were determined as reference standards. 2x2 contingency tables from the data were created and the diagnostic performance of the test by the superiority index (SI) was ranged.

Results: 13 articles and two abstracts were included. By the SI, "New criteria" proposed by Koh et al. had the best diagnostic performance for detecting CFLD (mean SI: 16.22, CI: 0.64-31) while transient elastography (TE) (mean SI: 10.66, CI: 1.40-27), and the combination of TE and TIMP-4 biomarker (mean SI: 8.84, CI: 0.03-35) proved to be the second and third best options.

Conclusion: Although "New criteria" was confirmed to be the best option, it consists of several subtests as well. The second best option transient elastography may be a promising alternative of Debray or Colombo criteria since its availability is good and its feasibility has been tested in several studies. It must be noted that our results are only qualitative and we plan to gain quantitative data as well.

Disclosure: Nothing to disclose

P0972 WITHDRAWN

P0973 WITHDRAWN

P0974

PERFORMANCE OF A 2D-SWE IMPLEMENTED ON A NEW ULTRASOUND SYSTEM FOR ASSESSMENT OF LIVER FIBROSIS USING TRANSIENT ELASTOGRAPHY AS THE REFERENCE METHOD

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Introduction: The aim of this prospective study was to evaluate the usefulness of 2D-SWE measurements obtained using the new UltraFastTM technology implemented on the Aixplorer MACH® 30 ultrasound system, for the noninvasive assessment of liver fibrosis, using Transient Elastography (TE) as the reference method.

Aims & Methods: 113 consecutive subjects were included in the study group, in whom liver stiffness (LS) was evaluated in the same session by means of two elastography techniques: TE (FibroScan, EchoSens) and 2D-SWE (Aixplorer MACH® 30 system, Supersonic Imagine). Reliable LS measurements were defined for TE as the median value of 10 measurements with an interquartile range/median ratio (IQR/M) <30% and for 2D-SWE the median value of 5 measurements performed as suggested by the manufacturer, via an intercostal approach in the right liver lobe, 1-2 cm under the liver capsule, in an area of parenchyma offside of large vessels, with an IQR/M < 30%. To discriminate between fibrosis stages by TE we used the following cut-offs: F2 - 7 kPa; F3 - 9.5 kPa and F4 - 12 kPa.

Results: Reliable LS measurements were obtained in 110/113 (97.3%) subjects by 2D-SWE and in 108/113 (95.5%) by TE, therefore the final analysis included 105 subjects. Based on TE [1] cut-off values we divided the rest of our cohort into 4 groups: F <2: 45/105 (42.8%); F2: 25/105 (23.8%); F3 = 11/108 (10.4%); F4 = 24/105 (23%). An excellent correlation was found between the LS values obtained by 2D-SWE and TE: $r=0.92$, $p < 0.0001$. The best 2D-SWE cut-off value for $F \geq 2=7$ kPa, $Se=83.3\%$, $Sp=95.5\%$, $PPV=96.2\%$, $NPV=76.8\%$, $AUROC=0.93$, $p<0.0001$; for $F4=10.8$ kPa, $Se=87.5\%$, $Sp=96.3\%$, $PPV=87.5\%$, $NPV=96.3\%$, $AUROC=0.93$, $p<0.0001$.

Conclusion: In our study, the best cut-off values were for $F \geq 2$, 7 kPa and for F4, 10.8 kPa. There was a very good performance of 2D-SWE and an excellent correlation between the LS values obtained by the two elastographic methods.

Disclosure: Nothing to disclose

P0975 WITHDRAWN

P0976

URINARY VOLATILE ORGANIC COMPOUNDS IN COMPARISON TO ALPHA FETOPROTEIN (AFP) IN HEPATOCELLULAR CARCINOMA. AN EXPLORATORY STUDY

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Introduction: Alpha fetoprotein (AFP) is no longer recommended for routine use in hepatocellular carcinoma (HCC) surveillance. On the other hand, the analysis of volatile organic compounds (VOCs) is emerging in

medical diagnostics for variety of diseases. VOCs are organic chemicals that can evaporate from liquid to gases. VOCs emerge from the cell membranes, following cellular damage, then find their way into the systemic circulation and finally excreted in the urine. Detection of urinary VOCs is of low cost ($\leq$ £30/sample). We compared AFP to chemical signatures of the urinary VOCs in HCC patients.

Aims & Methods: Ethical approval was granted by Coventry and Warwickshire research ethics committee (09/H1211/38). We collected 5 mls of urine from 31 HCC cases from January to June 2019. Male to female ratio was 5:1 and mean age was 72 years. Urine samples were left to freeze within 2 hours to -80°C . Analysis of the samples completed at the end of recruitment. Prior to analysis samples were left to thaw in a water bath at 50°C for 1 h. Urine was then placed into a Falcon conical centrifuge tube 50- mL with a modified cap with two slots to allow two solid phase micro-extraction tabs to be inserted to absorb gases from the head space of the samples. These tabs were analysed using an array of eight metal oxide gas sensors. Responses from the gas sensors to the urinary vapours were captured over a period of 180 seconds, then digitized and stored by computer software. The receiver operating characteristics (ROC) curves were calculated using established algorithm that was applied to different classes of data generated from an artificial radial basis function network (RBFN).

Results: The sensitivity of AFP alone in our study for HCC detection was 54.8% (raised AFP $>10\text{KU/L}$ in only 17 cases). When comparing urinary VOCs to AFP, they showed good discrimination in diagnosis of HCC. The sensitivity for detection of HCC with normal AFP was 68% (ROC Curve Area was 0.68, SE 0.06, 95% CI 0.54 to 0.81 and $P < 0.005$). The VOCs sensitivity in detection of HCC cases with raised AFP was 83%. (ROC Curve Area was 0.83, SE 0.05, 95% CI 0.73 to 0.93 and $P < 0.0001$).

Conclusion: Urinary VOCs could have a potential role in screening and surveillance of HCC. It is an attractive tool because it is non-invasive and has a low cost. Further validation from studies with larger sample size is required.

Disclosure: Nothing to disclose

P0977

URINARY ANALYSIS OF HEPATOCELLULAR CARCINOMA PATIENTS USING SOLID PHASE MICROEXTRACTION

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Introduction: Solid phase microextraction (SPME) is an analytical method for preconcentration of volatile organic compounds (VOCs) commonly used in analysis of biological samples. We applied SPME to study the urinary signatures of VOCs in hepatocellular carcinoma (HCC) patients.

Aims & Methods: Ethical approval was granted by Coventry and Warwickshire research ethics committee (09/H1211/38). We conducted a prospective recruitment between January to June 2019. Male to female ratio was 5:1 and mean age was 72 years (range 42 to 94). HCC cases were diagnosed as per EASL recommendations for 2018. Controls included patients that were suspected of cancer but had negative investigations. We collected 5 mls of urine from 31 HCC cases and 18 controls. The urine samples were left to freeze within 2 hours to -80°C . Analysis of these samples was then completed at the end of study recruitment. Prior to analysis samples were left to thaw in a water bath at 50°C for 1 h. Urine was then placed into a Falcon conical centrifuge tube 50-mL with a modified cap with two slots

to allow two solid phase microextraction tabs to be inserted to absorb gases from the head space of the samples. The tabs were then analysed using an array of eight metal oxide gas sensors. Responses from the gas sensors (1 to 8) to the urinary vapours were captured over a period of 180 seconds. The responses were digitized and stored by a computer software. The method of principal components analysis (PCA) was then employed to visualize these data.

Results: Data from the eight gas sensor responses were then demonstrated on a PCA plot, which made no assumptions about separation between classes. This visually showed that responses from the urinary VOCs of HCC patients were clearly differentiated from controls. This gives the impression that HCC has a potential urinary specific chemical signature. Urinary VOCs signature could potentially be used in the diagnosis of HCC.

Conclusion: Application of SPME urinary VOCs analysis in HCC patients has future potential as a diagnostic method. This will require further validation from other interested research groups.

Disclosure: Nothing to disclose

P0978

PROFILING OF URINARY PEPTIDES IN HEPATOCELLULAR CARCINOMA: AN EXPLORATORY STUDY

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Introduction: Hepatocellular carcinoma (HCC) is a frequent cause of death. HCC development is associated with liver inflammation, protein changes and fibrotic deposition. We investigated the low molecular weight urinary proteome in HCC to further advance our understanding of the disease.

Aims & Methods: We recruited 51 cases from university hospital Coventry/UK and Hannover medical school/Germany from January 2013 to June 2019. Ethical approval was granted from the appropriate bodies and consent was obtained from all participants. There were 20 HCC cases on background of liver cirrhosis (mean age of 60 years, 3 females and 17 males) and 31 controls (mean age 59 years, 11 females and 20 males). The controls included 9 non-alcoholic fatty liver disease, 13 non-alcoholic steatohepatitis and 9 healthy controls. 5 mls of urine was collected from each participant and frozen to -80°C . Analysis of the urine samples was completed by applying capillary electrophoresis (CE) coupled to mass spectrometry (MS). CE-MS is a hybrid technology using capillary electrophoresis (CE) for separation and mass spectrometry (MS) for mass detection enabling multidimensional analyte detection in complex biofluids. Raw CE-MS data processing and normalization procedures for inter-sample analysis were completed using computer software. Peptide sequences were resolved by tandem-MS and proteases potentially involved in HCC progression were matched to the N- and C terminal sequence motifs of the CE-MS identified peptide markers for HCC by the online software tool Proteasix.

Results: In silico protease prediction revealed that there were the following eight urinary proteases involved in the generation of the HCC-specific urinary peptide marker: Stromelysin-1 (MMP3), Collagenase 3 (MMP13), Kallikrein-6 (KLK6), Cathepsin D (CTSD) and Cathepsin E (CTSE) had increased activity whilst Meprin A subunit alpha (MEP1A), Cathepsin B (CTSB) and Granzyme A (GZMA) had reduced activity in HCC compared to controls.

Conclusion: Urinary CE-MS analysis identified eight proteases specific to HCC. These proteases could be associated with the development of HCC. Recent cancer research revealed that most of the proteases associated with cancer are involved in the degradation of the extracellular matrix and are also involved in the growth and spreading of cancer in the body.

Disclosure: Nothing to disclose

P0979

INDUCTION OF PROGRAMMED CELL DEATH (APOPTOSIS) IN HEPATOCELLULAR CARCINOMA BY USING A NOVEL COMBINATION OF PANOBINOSTAT AND BLEOMYCIN

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Introduction: Hepatocellular carcinoma (HCC) is the most common primary tumor of the liver and the third leading cause of cancer deaths worldwide. HCC cells show a high apoptotic capacity in earlier stages of carcinogenesis, in advanced stages they gradually develop a resistance towards apoptosis. This anti-apoptotic phenotype is associated with development and progression of HCC. Due to its chemoresistance, additional treatment must be taken into consideration. Histone deacetylase inhibitors promote apoptosis via the intrinsic apoptotic pathway, but at the same time these drugs sensitize tumour cells toward death ligands that activate the extrinsic apoptotic pathway. The chemotherapeutic drug bleomycin causes single- and double-stranded DNA breaks and produces reactive oxidative species leading to cell death. The aim of this study is to identify possible novel drug combinations in order to induce cell death in HCC cell lines and to extend the therapeutic repertoire for HCC.

Aims & Methods: The human hepatoma cell line HepG2 (p53wt) was incubated with serum concentrations of panobinostat (0.1-5 μ M) and bleomycin (2-10 μ M). DMSO treatment served as control. Cell death was measured after 12 and 24 h via flow cytometry using DAPI/Annexin V-APC staining. The caspase Inhibitor Z-Vad-FMK and the RIPK1 inhibitor Nec-1 were added to investigate the effects of treatment combinations on cell death. Caspase cleavage as well as levels of pro-/anti-apoptotic members of the Bcl-2 family were determined by Western blot.

Results: 24 h treatment with 0.1 μ M panobinostat induced a strong increase in cell death induction of up to 6.5-fold compared to the controls. 2 μ M bleomycin resulted in an increase of cell death of up to 4.5-fold. After incubation with a combination of panobinostat 0.1 μ M and bleomycin 2 μ M cell death rates were increased to up to 14.8-fold, indicating a synergistic effect. Cell death could effectively be blocked by Z-Vad-FMK indicating induction of apoptosis. Incubation with panobinostat, bleomycin and the combination of both therapeutics resulted in a cleavage of Caspases-3, -8, -9 and PARP, as well as in a downregulation of Bcl-XL as feature of apoptosis.

Conclusion: Our study demonstrates that novel combinations of already approved drugs like panobinostat and bleomycin could improve treatment options for HCC. Both drugs target different cellular pathways (panobinostat: HDAC; bleomycin: DNA double strand breaks), leading to synergistic effects and massive induction of apoptosis.

Disclosure: Nothing to disclose

P0980

FUSION NAVIGATION TECHNIQUE FOR MANAGEMENT OF DIFFICULT TO ACCESS HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular carcinoma (HCC) is one of the poorest prognostic solid cancer, representing about 90% of primary liver cancer. It is the third most common cause of cancer related mortality globally. Alternative to surgical resection of HCC, Percutaneous thermal ablation is broadly performed as a minimally invasive curative treatment for HCC. Sonography is the most universally used imaging technique for planning and performing thermal ablation in HCC patients due to its efficiency and safety. However, the presence of HCC nodules that are hardly visible on traditional sonography is a major drawback to its use during thermal ablation. Real-time image fusion (fusion imaging) or real-time virtual sonography is a new technology that has been developed. This new technology can overcome that weakness of traditional sonography.

Aims & Methods: This study aims to determine the value of fusion /navigation guided percutaneous thermal ablation in the management of hepatocellular carcinoma (HCC) that has poor conspicuity at conventional sonography.

This study included 42 HCC patients (BCLC A and B). Percutaneous radiofrequency ablation was done via real-time image fusion for the first group that contained 14 patients with HCC nodules that had poor conspicuity at conventional sonography (Study group), while Percutaneous radiofrequency ablation was done via traditional sonography for the second group that contained 28 patients with HCC nodules (Control group).

Results: The median time to reach the tumor was 1.85 ± 0.987 by using fusion navigation technique during radiofrequency ablation while it was 2.64 ± 1.28 minutes by using conventional ultrasound guided radiofrequency ablation ($P = 0.037$). As regard the ablation outcome after 1 month post procedure, by using fusion navigation technique 12 patients out of 14 patients was completely ablated while 14 patients out of 28 patients was completely ablated by using conventional ultrasonography ($P = 0.020$). As regard technical efficacy one year after the procedure, 12 patients out of 14 patients had complete response by using fusion navigation technique and only 13 HCC patients out of 28 patients had complete response by using conventional ultrasonography ($P = 0.018$). By using conventional ultrasound guided radiofrequency ablation, there was need to perform artificial ascites was in 2 patients while there was no need to use it during fusion navigation technique ($p = 0.56$). Kaplan-Meier survival analysis (Kaplan & Meier, 1958) was conducted to compare the two different interventions for their effectiveness in preventing recurrence. Participants in the study group had a median time to recurrence of more than one year while those in the control group had a median survival time of 12 months. A log rank test was conducted to determine if there were differences in the survival distribution for the different types of intervention. The survival distributions for both interventions were statistically significantly different, $\chi^2 = 10.12$, $p = 0.001$.

Conclusion: Fusion imaging-guided percutaneous RFA is a feasible and efficient method for treating patients with HCC undetectable by conventional abdominal ultrasonography. It can facilitate accurate interventional procedures for management of HCC.

Disclosure: Nothing to disclose

P0981

HEPATIC STEATOSIS IS ASSOCIATED WITH REDUCED RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CHRONIC HEPATITIS B INFECTION

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Introduction: Concomitant chronic hepatitis B infection (CHB) and non-alcoholic fatty liver disease (NAFLD) is common, but the implications of NAFLD on clinical outcomes of CHB, including hepatocellular carcinoma (HCC), are not well-investigated.

Aims & Methods: CHB patients [treatment-naïve and patients treated with nucleos(t)ide analogues (NA)] were recruited for transient elastography assessment for liver stiffness, and controlled attenuation parameter (CAP), a non-invasive quantification of steatosis, and were prospectively followed up for development of HCC. Steatosis and severe steatosis were diagnosed when CAP ≥ 248 dB/m and ≥ 280 dB/m respectively, and advanced fibrosis/cirrhosis was diagnosed when liver stiffness ≥ 9 kPa.

Results: Among 2403 CHB patients (55.6% male, median age 55.6 years, 57.1% NA-treated, median ALT 26 U/L) 48 patients developed HCC during a median follow-up of 46.4 months. Multivariate analysis showed increased CAP to be inversely associated with HCC development (OR 0.994, 95%CI 0.988-0.999). The cumulative probability of HCC was 2.88%, 1.56% and 0.71%, respectively for patients with no steatosis, mild-moderate steatosis, and severe steatosis, respectively ($p=0.01$). Sensitivity analysis among patients without advanced fibrosis/cirrhosis and NA-treated patients showed increased CAP remaining to be inversely associated with HCC (OR 0.991, 95%CI 0.983-0.999; and OR 0.993, 95%CI 0.987-0.999 respectively). The risk of HCC increased from 1.56% to 8.89% in patients without severe steatosis if advanced fibrosis/cirrhosis were present ($p<0.001$).

Conclusion: Reduced hepatic steatosis was significantly associated with a higher risk of incident HCC in CHB. Routine CAP and liver stiffness measurements can be important for risk stratification irrespective of fibrosis staging, and especially in on-treatment patients.

Disclosure: Nothing to disclose

P0982

ASSESSMENT OF THE TORONTO INDEX IN THE PREDICTION OF HCC INCIDENCE IN CIRRHOTIC PATIENTS

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Introduction: Cirrhosis requires regular and strict monitoring to prevent and detect the various complications. One of its complications is hepatocellular carcinoma (HCC). Current guidelines recommend twice-yearly ultrasounds for HCC surveillance in all patients with cirrhosis. However, the risk of HCC is known to vary with etiology, age gender and other factors. The Toronto index, using these different variables, aims to predict the risk of HCC in patients with cirrhosis.

Aims & Methods: This is a retrospective study of cirrhotic patients hospitalized in a gastroenterology department whose cirrhosis has been evolving for more than six months over a period of 5 years, from 2014 to 2019.

We excluded patients who had an inaugural HCC. The Toronto score was calculated for all patients. This score includes age, sex, etiology and platelets. The risk was then staged in low (Score < 120), intermediate (score between 120 and 240) and high (score > 240) according to the study conducted by Canadian experts from the University of Toronto.

Results: One hundred and one patients were included in this study, with a sex ratio (H / F = 50/51). The mean age was 59,3 years old. Forty-two patients had developed an HCC. Mean period between cirrhosis and HCC was 4.5 years. The etiologies of cirrhosis were: hepatitis C (43.5%), hepatitis B (16.8%), nonalcoholic steatopathy and alcoholic (16.3%), and dysimmunity (3.9%). For the group of patients who had HCC, 57% were male, the most common etiology was hepatitis C (59.5%), especially in the absence of antiviral treatment (44%), and secondly hepatitis B (21.4%). The Toronto score was calculated for all cirrhotic patients. A low risk of HCC (< 120) was noted in 11.8%, 42.75% had an intermediate risk and 45.5% a high risk. Of the patients who were at low risk, only one (8%) developed a HCC. For the intermediate risk group, the incidence of HCC was 34% and for the high risk group it was 56% over a period of 5 years.

Conclusion: The HCC incidence in cirrhotic patients depends on several factors including etiology. Toronto score is a validated score to predict HCC risk. The goal is to adapt the monitoring and thus to reduce the number of abdominal ultrasounds for patients with low risk.

Disclosure: Nothing to disclose

P0983

MORTALITY FOLLOWING LIVER BIOPSY TO DIAGNOSE METASTATIC MALIGNANCY IN THE LIVER

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Introduction: Liver biopsy is commonly undertaken to identify the aetiology of metastatic liver lesions. It is an invasive procedure with rare, but serious complications of severe bleeding, bile leak and infection. In our experience, newly diagnosed patients with metastatic cancer with a poor performance status may undergo these procedures without a realistic prospect of being offered oncological treatment.

Aims & Methods: Using Hospital Episode Statistics, liver biopsies undertaken for metastatic cancer (excluding primary liver cancer diagnoses) in England were examined. Risk factors for 14- and 30-day mortality were examined using multivariable logistic regression, adjusting for sex, age, ethnicity, comorbidity, deprivation, year of procedure, provider volume of liver biopsies (tertiles) and whether biopsies were performed as inpatient or outpatient.

Results: Between 2010 and 2019, 56,219 liver biopsies were performed in subjects for the diagnosis of metastatic cancer (50% male, median age 64 (IQR 54-73)). 61% (34,464) were performed in an outpatient/day-case setting. 4% (2,231) of subjects died within 14 days of biopsy and 11% (6,336) within 30 days. Of those who underwent inpatient biopsy (21,755), 8% (1,760) died within 14 days and 21% (4,502) died with 30 days. Subjects biopsied as an inpatient were 6 times more likely to die within 14 days and almost 5 times more likely to die within 30 days (odds ratios 6.32 (95%CI 5.70-7.02) and 4.76 (4.48-5.05) respectively). Females were less likely to die within 14 and 30 days (0.85 (0.78-0.93) and 0.85 (0.85-0.90) respectively). Compared to providers with a low volume of liver biopsies,

providers with a high volume were associated with a reduced risk of death at both 14 and 30 days (0.79 (0.69-0.91) and 0.81 (0.74-0.89) respectively). Older age, white compared to Asian ethnicity and higher deprivation were all associated with an increased risk of 30-day mortality.

31% of subjects went on to have chemotherapy (70% of those biopsied as an outpatient), while only 2% of those who died within 14-days and 5% of those who died within 30-days received chemotherapy. 1,831 (3.3%) of the cohort had a diagnosis of lymphoma recorded following a liver biopsy. **Conclusion:** 11% of subjects undergoing liver biopsy for metastatic cancer die within 30 days of this invasive procedure. Death is likely to be disease-related and factors such as poor performance status should be identified by clinical teams to prevent such interventions of little value and facilitate good end of life care.

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P0984 WITHDRAWN

P0985 WITHDRAWN

P0986

COMPARISON OF PROGNOSTIC MODELS IN PREDICTING SURVIVAL OF PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA UNDERGOING SORAFENIB TREATMENT: A MULTICENTER COHORT STUDY

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Introduction: Currently Sorafenib treatment is the gold standard therapy for patients with advanced hepatocellular carcinoma (HCC). To date, no widely validated scores are available to predict the overall survival of these patients.

Aims & Methods: The aim of our study is to evaluate the accuracy of the current available prognostic scores for HCC to predict the overall survival of patients with advanced HCC treated with Sorafenib. We included all patients undergone Sorafenib treatment belonged to the prospective multicenter cohort of the Italian Liver Cancer (ITA.LI.CA.) database. We selected clinical data from the visit before treatment administration. Patients lost at follow-up were excluded. We assessed the performance of several prognostic scores [Barcelona Clinic Liver Cancer- BCLC, Italian Liver Association (AISF)-BCLC, TNM, Hong-Kong Liver Cancer- HKLC, Italian Liver Cancer score- CLIP, ITA.LI.CA. Prognostic score, Okuda score, Albumin-Bilirubin (ALBI) score, GRETCH score] through a univariate Cox regression model evaluating the C-index (Harrell's C) and the Akaike Information Criterion (AIC) of each prognostic score. A high C-index and a low AIC were indicator of good accuracy of the score.

Results: One-thousand and one-hundred and twenty-nine (1129) patients were included. The mean age of the patients was 61.6 years. A total of 80.8% of the patients enrolled were male. Seven-hundred and eighty-nine patients died during a median follow-up period of 15 months. The median period of Sorafenib administration was 4 months. During the follow-up 63.1% of the patients experienced a HCC progression. All the prognostic scores were able to independently predict the overall survival ($p < 0.001$) at

univariate analysis, except for ALBI score ($p = 0.152$). The CLIP score yielded the higher accuracy (C-index: 0.608, AIC: 6565) followed by the ITA.LI.CA. prognostic score (C-index: 0.594, AIC: 8569) and the Okuda score (C-index 0.579, AIC 7257) among the scores evaluated.

Conclusion: The overall survival of patients included in ITA.LI.CA. database undergoing Sorafenib treatment is slightly higher than that reported in the current literature. To date, the CLIP score and the ITA.LI.CA. Prognostic score showed the highest accuracy in predicting the overall survival of these patients, although it remains poor. Further studies are needed to investigate the prognostic role of other clinical variables.

Disclosure: Nothing to disclose

P0987

PROGNOSTIC PERFORMANCE OF TEN NONINVASIVE LIVER FUNCTION TESTS IN PATIENTS WITH HEPATOCELLULAR CARCINOMA PROPOSED TO SYSTEMIC TREATMENT WITH SORAFENIB

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Introduction: Various noninvasive liver function tests have been proposed to assess hepatic reserve (Child-Turcotte-Pugh (CTP); albumin-bilirubin [ALBI] grade, platelet-albumin-bilirubin [PALBI] grade, model for end-stage liver disease [MELD], fibrosis index based on 4 factors [FIB-4], aspartate aminotransferase-to-platelet ratio [APRI], Lok index, cirrhosis discriminant index [CDS], King's score, and Göteborg University Cihhosis Index [GUCI] in chronic liver disease). However, their performance to predict the prognosis of patients with hepatocellular carcinoma (HCC) is unknown.

Aims & Methods: We aimed to elucidate the prognostic role of ten currently used hepatic function models in patients with advanced stage HCC proposed to systemic treatment with Sorafenib. Between 2009 and 2017, patients with HCC submitted to systemic therapy were retrospectively analyzed. For each patient, baseline patient characteristics, tumor status, and noninvasive hepatic function models at the drug starting time were collected. Each model was categorized into three classes (Grade 1/2/3). Cox proportional hazards model was used to identify independent survival predictors.

Results: We evaluated 61 patients with a mean age of 64.1 ± 13.6 years, 82% of the male gender. The major causes of liver disease were alcohol (37.7%) and HCV infection (24.6%). Sorafenib was the first therapeutic option in 52.5% of the cases. The most frequent adverse effects were diarrhea (32.8%) and hand-foot syndrome (26.2%). The median survival after starting sorafenib was 9 (IQR 3-15) months. The mortality rate after one year of treatment was 62.3%. When the scores were analyzed regarding survival significant differences were found in the ALBI score (stage 1/2/3 - 8/9/2 months; $p = 0.04$) and the CTP (stage 1/2 - 10/3 months, $p < 0.01$). In the covariate-adjusted multivariate Cox regression model, we found that ALBI grade 3 (vs. grade 1/2) was significantly associated with the survival estimate (HR 3.32; CI95% 1.14 - 9.61; $p = 0.03$).

Conclusion: Among the ten noninvasive tests of hepatocellular function, only the ALBI score independently predicted a lower survival for HCC patients treated with sorafenib. This score can be used routinely as a prognostic prediction tool in patients proposed to sorafenib treatment, especially in those patients that don't meet the strict clinical criteria presented in international guidelines (such as Child-Pugh B patients).

Disclosure: Nothing to disclose

P0988

PROGRESSION-FREE SURVIVAL IS A CONSISTENT SURROGATE ENDPOINT OF OVERALL SURVIVAL IN IMMUNOTHERAPY TRIALS OF ADVANCED HEPATOCELLULAR CARCINOMA: A META-ANALYSIS

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Introduction: Radiology-based outcomes (progression-free survival (PFS), time-to-progression and objective response rate) are widely used as surrogate endpoints in oncology trials. We aimed to assess the surrogate relationship between PFS and overall survival (OS) in clinical trials of systemic therapy for advanced hepatocellular carcinoma (HCC).

Aims & Methods: A search of databases (PubMed, ASCO and ESMO Meeting Libraries and Clinicaltrials.gov) for trials of systemic therapy for advanced HCC reporting both results for OS and PFS was performed. Individual data were extracted for each trial from the Kaplan-Meier curves of PFS and OS. We performed a random effects meta-analysis to obtain a summary median PFS and OS.

The surrogate relationships of median, first (Q1), third quartile (Q3) and restricted mean survival time (RMST) PFS for OS were evaluated by the coefficient of determination R^2 . Heterogeneity was explored by meta-regression.

Results: We identified 49 trials, 11 assessing immune checkpoint inhibitors (ICIs) and 38 multikinase inhibitors (MKIs). Overall, R^2 between median PFS and median OS was weak (0.20). The surrogacy varies between treatment classes and different time points of PFS. In ICI trials, the correlations between Q1- PFS and Q1- OS and between 12-month-RMST PFS and 12-month-RMST OS were high ($R^2 = 0.89$ [95% Confidence Interval 0.78-0.98] and 0.80 [0.63-0.96], respectively).

In MKI trials, the correlation between PFS and OS remains weak, regardless of the time-point of PFS. Interaction by meta-regression confirmed the robustness of the results.

Conclusion: In trials of systemic therapies for advanced HCC, the surrogate relationship between PFS and OS is highly variable depending on different treatment classes (ICIs and MKIs) and different time-points of evaluation. Q1-PFS and 12-month-RMST PFS are robust surrogate endpoint for OS.

Disclosure: Nothing to disclose

P0989

OPTIMIZING SEQUENTIAL SYSTEMIC THERAPIES FOR ADVANCED HEPATOCELLULAR CARCINOMA: A DECISION ANALYSIS

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Introduction: An optimal sequential systemic therapy for advanced hepatocellular carcinoma (HCC) has not been discovered. We developed a decision model based on available clinical trials to support physicians in identifying an optimal risk/benefit strategy for sequences of novel systemic agents.

Aims & Methods: A Markov model was built to simulate overall survival (OS) among patients with advanced HCC. Three first-line treatments (single-agent Sorafenib or Lenvatinib, and a combination of Atezolizumab plus Bevacizumab) followed by five second-line treatments (Regorafenib, Cabozantinib, Ramucirumab, Nivolumab, and Pembrolizumab) were compared in fifteen sequential strategies. Health states were defined for initial treatment, cancer progression, and death. The likelihood of transition between states was derived from clinical trials. Deterministic and probabilistic analyses were conducted to assess model uncertainty. Life-year gained (LYG) was the main outcome. Rates of severe adverse events (SAEs) ($\geq$ grade 3) were calculated. The incremental safety-effectiveness ratio (ISER) of the two best sequential treatments was calculated as the difference in probability of SAEs divided by LYG.

Results: Compared with first-line Sorafenib followed by second-line Ramucirumab (median OS, 18 months), first-line Lenvatinib followed by second-line Nivolumab (median OS, 27 months) was the most effective, producing a LYG of 0.75 and a number needed to treat of 5. Sequential strategies with second-line Nivolumab or Pembrolizumab were the safest (SAEs ranging from 40-64%). The ISER of Lenvatinib followed by Nivolumab and Atezolizumab plus Bevacizumab followed by Nivolumab was 32% of SAEs per LYG. Deterministic and probabilistic analyses confirmed the robustness of these results.

Conclusion: Single-agent, first-line Lenvatinib followed by Nivolumab or Pembrolizumab were identified as optimal sequential strategies for advanced HCC. These estimates should be considered for future clinical trials.

Disclosure: Nothing to disclose

P0990

RISK OF OCCURRENCE AND RECURRENCE OF HEPATOCELLULAR CARCINOMA IN 349 PATIENTS WITH LIVER CIRRHOSIS AND HEPATITIS C VIRUS INFECTION GENOTYPE 1 B TREATED WITH SOFOSBUVIR+LEDIPASVIR± RIBAVIRIN

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Introduction: Data from literature regarding the risk of recurrence and occurrence of hepatocellular carcinoma (HCC) in patients with liver cirrhosis and hepatitis C virus(HCV) infection treated with direct acting antiviral agents (DAA) are conflicting [1-5].

Aims & Methods: The aim of this study was to evaluate the prevalence and risk factors for occurrence and recurrence of HCC in patients treated with Ledipasvir + Sofosbuvir ±Ribavirin(LDV/SOF±RBV). We conducted a multicentric retrospective study including 349 patients with decompensated liver cirrhosis and HCV genotype 1b infection treated with LDV/SOF±RBV for 12-24 weeks.

The first group included 18 patients with treated HCC prior to DAA therapy. They were followed for tumor recurrence every 3-4 months, with contrast-enhanced CT and/or MRI. The second group consisted of 321 subjects without a history of HCC, monitored for HCC occurrence by liver ultrasonography every 6 months. The median follow-up period was 20 months (5÷24).

Results: In the 18 subjects, 6 (33.3%) were women and 12 (66.6%) men, with a median age of 65 (48÷81 years).Sustained viral response at 12 weeks (SVR12) was obtained in 12 patients (66.7%). The HCC recurrence appeared in 8 subjects (44.4%). The median elapsed time between the last HCC procedure and the start of DAA treatment was 20 months (range 3-60), between last procedure for HCC and recurrence was 25 months (range 13-39) and between start of DAA therapy and recurrence was 12 months (range 6-12). Lack of SVR 12 was the only predictive factor for recurrence: 50% in patients with recurrence vs 80% in those without(p=0.034).

HCC occurred in 15/321 subjects (4.7%). We found the following risk factors for HCC occurrence: poor liver function (higher Child Pugh score (p=0.007), low albumin levels (p=0.001), high bilirubin levels (p=0.01)) and low platelet count (p=0.001) (Table 1).

Parameter	No HCC occurrence (306)	Occurrence (15)	p-value
Male sex n (%)	122 (40.4 %)	8 (53.8%)	0.393
Age (years)	61, 35-83	67, 47-71	0.506
Initial HCV-RNA load (IU/ml)	247000, 55-7276049	76200, 36700-880793	0.460
DAA-HCC interval (months)	-	6, 3-18	NA
Platelet count at baseline (x 10 ⁹ /L)	95, 23-491	56, 10-130	0.001
AST at baseline (IU/L)	77, 20-396	82, 41-189	0.566
Total bilirubin at baseline (mg/dl)	1.6, 0.3-9	2.64, 1.2-3.8	0.014
Albumin at baseline (g/dl)	3.4, 1.6-5.3	2.8, 1.8-3.2	0.001
AFP at baseline (ng/ml)	9.1, 0-257	34.3, 5.2-82	0.075
HBV co-infection	4.7%	0%	0.424
Diabetes mellitus N (%)	76 (24.9 %)	2 (15.4 %)	0.742
Comorbidities N (%)	155 (50.8 %)	7 (46.2 %)	0.784
Child Score (%) A/B/C	42.1/52.5/5.4	0/84.6/15.4	0.007
MELD Score at baseline	10.49, 6.14-19.71	13.23, 8.18-17.84	0.083
Clinical evolution at SVR - improvement N (%)	167 (54.5 %)	12 (76.9 %)	0.475
SVR N (%)	292 (89.2 %)	12 (76.9 %)	0.171

[Table 1.Clinical and paraclinical features in the group of patients with and without HCC occurrence]

Following the MELD score at initiation,there is no statistically significant

difference. However, there were no differences in the response to LDV/SOF therapy, with a SVR12 rate similar between the two groups (76.9% for those with occurrence vs 89.2% for patients without occurrence, p=0.171).

Conclusion: The recurrence rate of HCC in cirrhotic patients was 44.4% (30.6/100 patient-year). These patients had a low rate of SVR12 (66.7%), and a favorable evolution of paraclinic parameters. The occurrence rate of HCC was 4.7% for a median follow-up period of 20 months. The predictive factors for the HCC occurrence were a lower platelet number and an impaired liver function (decreased albumin and increased bilirubin at the beginning of treatment, which means a higher Child Pugh score).

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Disclosure: Nothing to disclose

P0991

NON-INVASIVE SERUM TESTS - PREDICTORS OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION AND POSTHEPATECTOMY LIVER FAILURE IN PATIENTS WITH CIRRHOSIS COMPLICATED WITH HEPATOCELLULAR CARCINOMA

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Introduction: Hepatic resection is one of the curative therapeutic options in the management of hepatocellular carcinoma (HCC). Given the fact that HCC occurs most commonly in the cirrhotic liver, the stage of liver disease is very important in establishing the resection criteria, based on tumor size and the presence of portal hypertension (PHT), measured by hepatic venous pressure gradient (HVPG).

The purpose of the study was to evaluate whether serum liver tests may

identify the patients with clinically significant portal hypertension (CSPH), and thus at risk to develop post-hepatectomy liver failure (PHLF). Their performances were compared with liver stiffness measurement (LSM).

Aims & Methods: 111 patients with compensated cirrhosis and HCC referred to hepatic resection between 2015 and 2020 in the Regional Institute of Gastroenterology and Hepatology Cluj-Napoca were included. Presence of CSPH was defined as: HVPG ≥ 10 mmHg or presence of esophageal varices, splenomegaly and thrombocytopenia ($< 100.000/\text{mm}^3$). The non-invasive serum tests were: APRI, FIB-4, NLR, eLIFT, ALBI. The performance of non-invasive tests in predicting CSPH and prognosis were assessed by AUROC curves.

Results: Among the included patients (65 ± 7 years; 24% alcohol, 45% VHC, 18% VHB and 13% other etiologies) 34% had CSPH, 31% had esophageal varices and 26% had splenomegaly and thrombocytes $< 100.000/\text{mm}^3$. APRI, FIB4 and eLIFT were good predictors of CSPH (AUROC=0.87, 95%CI:0.79-0.95; $p < 0.05$; AUROC=0.88, 95%CI:0.81-0.96; $p < 0.05$ and AUROC=0.83, 95%CI:0.73-0.92; $p < 0.05$, respectively). Still, LSM had the best performance to predict CSPH (AUROC=0.913, 95%CI:0.84-0.98; $p < 0.05$). ALBI and NLR were not capable of predicting CSPH.

Regarding the prediction of PHLF, although the statistical significance was not reached, LSM, APRI and FIB-4 have a tendency to predict it.

Conclusion: Liver stiffness and non-invasive tests such as APRI, FIB-4 and eLIFT may identify patients with clinically significant portal hypertension in patients with HCC submitted to hepatic resection, but are not capable to predict prognosis in this clinical setting.

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P0992

IS IT TIPS ASSOCIATED WITH INCREASED RISK OF HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS?

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Introduction: Clinically significant portal hypertension (CSPH) is associated with an increased risk of developing hepatocellular carcinoma (HCC). Although trans-jugular intrahepatic shunt (TIPS) significantly decreases portal hypertension and the recurrence of its complications, previous studies have shown an increased risk of developing HCC in this population.

Aims & Methods: The aim of this study was to compare the risk of developing HCC in cirrhotic patients with CSPH that undergo TIPS procedure versus a control group of patients with cirrhosis and CSPH. 104 cirrhotic patients who underwent TIPS procedure for the treatment

of refractory ascites or for secondary prophylaxis of esophageal variceal bleeding were included and followed-up for a median of 27.64 ± 23.9 months. 450 cirrhotic patients who had the hepatic venous gradients (HVPG) measured between 2012 and 2020 at the Regional Institute of Gastroenterology and Hepatology in Cluj-Napoca and found with CSPH (HVPG > 10 mmHg) were included as a control group (median follow-up 11.50 ± 13.5 months). TIPS patients were followed-up at 1 month, 3 months and 6 months afterwards, while the rest of the patients were screened for HCC every 6 months.

Results: Compared to the control group, TIPS patients were younger (53.65 vs 57.13 y, $p=0.003$), had higher percentage of alcohol induced cirrhosis (56.7% vs 44.1% , $p < 0.001$) and more advanced liver disease (Child-Pugh B 50.5% vs 28.5%). At the end of follow-up, 3.8% of TIPS patients had developed HCC compared to 1.6% ($p=0.133$) in the control group. The time to HCC was longer in TIPS patients (19.33 months vs 15.4 months). The patients that developed HCC in the TIPS group had a more advanced liver disease (Child-Pugh C 75% vs 28.6%) in comparison to the control group. A HVPG higher than 22mmHg was associated with an increased risk of developing HCC for the patients in the control group (OR=3.69 [$1.1, 12.34$], $p=0.039$).

Conclusion: Although cirrhotic patients with CSPH that undergo TIPS have a more advanced liver disease, they do not show a statistically significant increased risk of developing HCC. Patients with an HVPG > 22 mmHg and more advanced liver disease have a higher risk of developing HCC.

Disclosure: Nothing to disclose

P0993

CHARACTERIZATION AND NATURAL HISTORY OF CONGENITAL INTRAHEPATIC PORTO-SYSTEMIC SHUNTS

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Introduction: Congenital intrahepatic portosystemic shunts are rare vascular malformations in which abnormal communications are created between the portal veins and the hepatic veins and the inferior vena cava system. Diagnosis is made by prenatal or postpartum ultrasound. Published data regarding presentation, symptoms and prognosis is scarce. The aim of this study was to better understand the natural history and the course of the intrahepatic portosystemic shunts.

Aims & Methods: Data were collected from children in two medical centers who were diagnosed with congenital intra-hepatic portosystemic shunts on either pre-natal or post-natal sonographic screening. The subjects' medical information was collected including demographics, medical background, and sonographic and clinical outcome. Blood test results including biochemical analysis (ammonia) and liver function tests were documented, as well as the sonographic dimensions of the shunt vessels and the spleen size. All the data were analyzed using various statistical methods.

Results: Twenty-three children with portosystemic shunts were detected. However, 8 children were excluded from the study since records and follow up were insufficient. Fifteen patients were included in the study that all had more than one ultrasound and repeated blood tests. Six were female and all had intra-hepatic shunt diagnosed either by prenatal screening (10) or postnatal abdominal ultrasonography (5). Shunt closure was observed in all children within mean of 114.31 ± 115.05 days (median 84). There was no correlation between liver enzymes, ammonia, and ultra-

sound vascular and splenic diameters or to time to closure. None of the children had any hepatic or other sequela.

Conclusion: Our study suggests that congenital intrahepatic portosystemic shunt is a benign, self-limiting condition in which no correlation between the size of the shunt and the blood ammonia level to the outcome of the shunt was found. This is the first study which correlated radiological measures to outcome. These results suggest that the treating physician should reassure families and conduct minimal follow-up and interventions in children with such condition. Further, larger and prospective studies should be done to corroborate these conclusions.

Disclosure: Nothing to disclose

P0994 WITHDRAWN

P0995

RE-CAPTURING A LOST POPULATION - THE BENEFITS OF A NURSE-DELIVERED HCV COMMUNITY CIRRHOSIS CLINIC

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Introduction: The current landscape of service provision for patients with liver disease does not match that of disease burden. A North London-based drug and alcohol dependency unit ('Better Lives') provides blood borne virus (BBV) screening and opioid substitution therapy (OST) as well as Hepatitis C Virus (HCV) treatment. These patients are often complex with marginalised social needs, have chaotic lifestyles and don't engage with conventional care models.

Aims & Methods: We aimed to describe the demographics of a cohort of patients seen in a novel community outreach clinic (OC). Approximately 1000 patients per year receive OST from 'Better Lives' via a multidisciplinary clinic with doctors, nurses and recovery workers. 117 (11.7%) screened positive for chronic HCV. 22 (18.8% of chronic HCV patients, 2.2% of those receiving OST) with advanced liver fibrosis or cirrhosis (F3/F4) were referred to OC between November 2018 and September 2019. We used electronic hospital records to assess 'Did Not Attend' (DNA) rates to outpatient appointments (OPA) and emergency department (ED) attendances prior to review in OC and completion of key investigations afterward.

Results: 22 patients referred to OC in the study period (median age 52 (IQR 46.3 - 57), 81.8% male, 40.9% white). 14 patients (63.6%) attended. Chronic HCV primary aetiology in 12 (54.5%), 11 (50%) self-reported ongoing alcohol intake and 4 (18%) were people who inject drugs (PWID). Median liver stiffness 19kPa (IQR 12.95 - 36.1). 12 (54.5%) did not have registered GPs. 15 (68.2%) DNA hospital appointments prior to OC clinic.

Conclusion: This is the first UK-based nurse-delivered community liver cirrhosis outreach clinic aimed to improve treatment and supportive medical care and offer a link to hospital cirrhosis services. We re-engaged two-thirds of complex marginalised patients with advanced fibrosis via OC that would otherwise have been lost to follow up. Patients attending OC had an average of 2 prior DNA to hospital OPA and 6 ED attendances. 35% and almost 50% of patients had their surveillance US abdomen and gastroscopies, respectively, following attendance to OC compared with only 12% who did not attend. Further work to investigate if a community based liver outreach clinic can improve the trajectory of marginalised patients is required.

Disclosure: Nothing to disclose

	All F3/F4 patients referred (n = 22)	Patients attending OC (n = 14)	Patients not attending OC (n = 8)
Age (median, IQR)	52 (46.3 - 57)	53.5 (45 - 57.75)	50.5 (28.5 - 53)
Gender (Male), n (%)	18 (81.8)	11 (78.6)	7 (87.5)
HCV Aetiology, n (%)	12 (54.5)	9 (64.2)	3(37.5)
Ongoing alcohol intake, n (%)	11 (50)	11 (78.6)	0 (0)
Prior DNA OPAs, mean (SD)	2.14 (2.14)	2.07 (1.64)	2.25 (2.96)
Prior ED attendances, mean (SD)	5.05 (6.94)	6 (7.2)	3.38 (6.57)
US Abdomen after OC, n (%)	7 (31.8)	6 (42.86)	1 (12.5)
Gastroscopy after OC, n (%)	6 (27.3)	5 (35.71)	1 (12.5)

[Table 1. Comparison between patients attending outreach clinic and not attending]

P0996

NON-INVASIVE FIBROSIS TESTS IN IDENTIFYING ADVANCED LIVER DISEASE TO FACILITATE REFERRAL TO LIVER CLINICS - A US VETERAN COHORT ANALYSIS

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Introduction: Advanced liver disease (ALD), defined as presence of bridging fibrosis (fibrosis stage F3) and cirrhosis (fibrosis stage F4), indicates increased risk of liver-related morbidity and mortality. Identification of ALD in a primary care (PC) setting can expedite referral to specialist care. Vibration controlled transient elastography (Fibroscan) is commonly used to determine liver fibrosis stage but is not universally available. Non-invasive fibrosis tests (NITs) like fibrosis-4 score (FIB-4), aspartate transaminase to platelet count ratio index (APRI) and NAFLD fibrosis score (NFS) can be used to identify ALD in resource-limited settings. No large studies have evaluated the role of NITs in identification of ALD and its role in guiding PC referral to hepatology service.

Aims: We aimed to study the accuracy of FIB-4 and APRI to predict ALD and cirrhosis in patients referred to hepatology clinic from PC. In addition to FIB-4 and APRI, NFS was studied in a sub-group of patients with non-alcoholic fatty liver disease (NAFLD).

Methods: In a US veteran cohort, we analyzed all patients referred to hepatology clinic from PC service (between Jan 2017 and March 2019), and who had a fibroscan. Baseline demographic features were studied, and NITs were compared.

Results: In a US veteran cohort, we analyzed all patients referred to hepatology clinic from PC service (between Jan 2017 and March 2019), and who had a fibroscan. Baseline demographic features were studied and NITs were compared.

Of 545 patients studied, mean age was 60.8 ± 11.0 years, 91.6% males, 70.5% Caucasians and 26.8% African Americans. Predominant etiology of liver disease was chronic hepatitis c (45.1%) followed by NAFLD (29.7%). Mean BMI of the group was 30.1 ± 6.8; 45.9% obese and 28.4% overweight. Based on fibroscan liver stiffness measurement (LSM), 44% had advanced fibrosis (LSM ≥ 9 Kpa) and 22.9% had cirrhosis (LSM ≥ 13.5 Kpa).

The AUROCs ($\pm$ SE) for FIB-4 and APRI for predicting ALD were 0.701 ($\pm$ 0.23) and 0.685 ($\pm$ 0.23) and for predicting cirrhosis were 0.761 ($\pm$ 0.24) and 0.736 ($\pm$ 0.25) respectively (figure 1). At a cut off of 3.25, FIB-4 was 89.7% specific for predicting cirrhosis ($p < 0.001$) and 92.5% specific in predicting ALD ($p < 0.001$).

On subgroup analysis of patients with NAFLD, FIB-4 had higher predictive accuracy than NFS for predicting ALD (0.732 and 0.704, $p < 0.001$) and cirrhosis (0.782 and 0.716, $p < 0.001$) (figure 2). In this subgroup, at a cut off of 3.25, FIB-4 was 92.8% specific for predicting cirrhosis ($p < 0.001$) and 94.1% specific in predicting ALD ($p < 0.001$).

Conclusion: In a primary care setting, NITs can be used to identify patients with ALD and to expedite referral to hepatology clinic. Among the NITs, FIB-4 has the highest predictive accuracy to predict ALD and cirrhosis, irrespective of etiology of liver disease.

Disclosure: Nothing to disclose

P0997

TELEMEDICINE IN HEPATOLOGY AND PATIENT SATISFACTION: LESSONS FROM THE COVID-19 PANDEMIC

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Introduction: The COVID-19 pandemic poses a massive challenge to healthcare systems and an opportunity for them to reinvent themselves. Telephone consultation (TC) seems a reasonable approach, being recommended by different societies as an alternative to assist patients with liver disease during pandemic crisis.¹ Despite physicians' concerns related to uncertain prognostic consequences of using telemedicine, it is also important to understand patient's perspective about TC.

Aims & Methods: Outpatients followed in hepatology consultation submitted to TC during an initial period of 5 weeks were contacted again and invited to answer an adapted version of the Telemedicine and Satisfaction Questionnaire² and open-ended questions regarding patient global assessment of TC. Only patients with at least one outpatient face-to-face consultation (FFC) were considered. The recorded data included demographic and clinical characteristics, survey answers, distance from home to hospital and working time usually missed in FFC. Primary endpoints were the frequency of satisfied patients with TC and patients' availability to be assisted through TC in the future (answered "agreed" or "strongly agreed" on 4-point Likert scale). Secondary endpoints were the possible factors associated with better satisfaction with TC and patients' burden in FFC.

Results: From a total of 78 outpatients submitted to TC, 68 (87.2%) answered the call and agreed to respond to the survey (35 [51.5%] were men; median age was 59.5 years [IQR 54.3-69.5]). Alcoholic liver disease, nonalcoholic fatty liver disease and primary biliary cholangitis were the most common diagnosed liver diseases: 28 (41.1%), 9 (13.2%) and 8 (11.7%), respectively.

Sixty-one (89.7%) patients were satisfied with TC and 46 (67.6%) considered TC as a reasonable way to be attended to in the future. A higher educational level (secondary and higher education vs primary education) was associated with more availability for assistance through TC in the future (83.3% vs 55.2%, $p = 0.014$).

Median distance from home to hospital was 39.5 km (IQR 20.0-61.5) and 29.4% (20) of the patients (or their caregivers) usually have to miss work (13.2% [9] need to take a day off) to go for a FFC.

Cost savings, decreased travel and waiting times were the main advantages pointed out by patients; lack of face-to-face interaction the main disadvantage. Intercalate TC and FFC was the main patients' suggestion regarding this topic.

Conclusion: These results suggest that patients with liver disease were generally satisfied with TC and most of them would consider to be assisted this way in the future. Further efforts to investigate physicians' TC perceptions, patients' prognostic outcomes and what kind of patients are appropriate to be assisted through TC should be explored.

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Disclosure: Nothing to disclose

P0998

PEMBROLIZUMAB AS SECOND-LINE THERAPY OF HEPATOCELLULAR CARCINOMA: A COST-EFFECTIVENESS ANALYSIS FROM THE UNITED KINGDOM HEALTHCARE PERSPECTIVE

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Introduction: Recently, checkpoint inhibitors have been approved for the second-line therapy of hepatocellular carcinoma (HCC) in patients who previously received sorafenib. Pembrolizumab has demonstrated substantial anti-tumor activity and favorable toxicity profile as second-line treatment of HCC. However, considering the high cost of pembrolizumab, there is a need to assess its value by considering both efficacy and cost. We aimed to evaluate the cost-effectiveness of pembrolizumab vs. placebo as second-line therapy in hepatocellular carcinoma (HCC) patients from the United Kingdom (UK) healthcare perspective.

Aims & Methods: A Markov model was developed to compare the lifetime cost and effectiveness of pembrolizumab with those of placebo as second-line treatment of HCC using outcome data from the KEYNOTE-240 randomized control trial. Life-years, quality-adjusted life-years (QALYs), lifetime costs, and incremental cost-effectiveness ratio (ICER) were estimated, at a willingness-to-pay threshold of £30,000 to £70,000 per QALY. Univariable, 2-way, and probabilistic sensitivity analyses were performed to evaluate the model uncertainty. Cost threshold analysis was also performed.

Results: In the base-case analysis using data from KEYNOTE 240 trial, pembrolizumab provided a gain of 0.15 life-year and 0.14 QALY with additional cost of £30,873. The ICER was £184,301 for pembrolizumab compared with placebo and best support care. Overall survival hazard ratio (0.78; 95% CI: 0.61-1.00), cost of pembrolizumab (£3,682 per cycle, range: 2946 - 4418), and utility of placebo (0.76, range: 0.59-0.93) had the strongest influence on ICER. The ICER for pembrolizumab was > £100,000 per QALY in all of our univariable and probabilistic sensitivity analyses. In cost-threshold analysis, the price of pembrolizumab would have to be priced 57.6% lower to be cost-effective considering a willingness to pay of £70,000 per QALY.

Conclusion: At current cost, pembrolizumab is not a cost-effective second-line therapy of HCC at a willingness-to-pay threshold from £30,000-£70,000 per QALY in the UK.

Disclosure: Nothing to disclose

P0999 WITHDRAWN

P1000

RHEOLOGICAL PROPERTIES OF BILE IN PATIENTS WITH NONALCOHOLIC STEATOHEPATITIS AND THYROID GLAND DYSFUNCTION

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Introduction: Thyroid gland plays an essential role in lipid and carbohydrate metabolism, in particular cholesterol metabolism, obesity and insulin resistance development as well as reduction of gluconeogenesis. Due to the increasing incidence of thyroid gland hypofunction the relationship between hypothyroidism (HT) and rheological properties of bile in patients with nonalcoholic steatohepatitis (NASH) should be studied.

Aims & Methods: To assess the changes in bile acids (BA) composition in patients with NASH combined with HT.

135 adult patients (35-60 years; mean age 47.5 ± 4.1 years) were involved in to the study. 73 patients with NASH and HT were allocated to the I group. The control group (group II) included 62 patients with NASH and without concomitant HT. The groups were statistically comparable in age and sex ($p = 0.52$). The bile was obtained after intubation of the duodenum under the ultrasound control. The spectrum of BA and bile properties were assessed using photocalorimetry. To evaluate the colloidal stability of the bile, the ratio of taurochenodeoxycholic acid (TCDCA) and taurodeoxycholic acid (TDCA) to taurocholic acid (TCA) and the ratio of glycochenodeoxycholic acid (GCDCA) and glycodeoxycholic acid (GDCA) to glycocholic acid (GCA) were calculated. The level of thyroid stimulating hormone (TSH) was determined in blood due to the electrochemiluminescence method. The correlation between HT and BA spectrum were estimated.

Results: The analysis of BA in patients with HT showed a significant increase of both cholic acid (CA) level (group I - 49.1 ± 1.2 mg% vs group II - 6.9 ± 0.4 mg%, $P < 0.05$) and deoxycholic acid (DCA) level (I group - 56.2 ± 2.1 mg% vs group II - 33.2 ± 1.3 mg%, $P < 0.05$). Also, group I showed decreased levels of TCA (group I - 54.8 ± 1.2 mg% vs group II - 165.6 ± 2.4 mg%, $P < 0.001$), and increased levels of GCA (group I - 254.9 ± 6.2 mg% vs group II - 178.9 ± 2.6 mg%, $P < 0.001$). The assessment of colloidal stability revealed decreased ratios of TCDCA + TDCA to TCA and GCDCA + GDCA to GCA in patients with HT ($P < 0.05$ in both cases). The analysis of the correlation between TSH and the BA spectrum showed a strong direct correlation between the levels of TSH and both CA ($r = 0.74$; $P < 0.05$) and TCA ($r = 0.67$; $P < 0.05$).

Conclusion: Decreased coefficient of conjugation and hydroxylation, as well as the levels of glycoconjugates and tauroconjugates of the bile in patients with NASH combined with HT suggests the possible influence of hypothyroidism on colloidal properties of bile and thus indicates on an increased risk of gallstones formation.

Disclosure: Nothing to disclose

P1001

RELATIVE ACTIVITY OF GUT BACTERIAL BILE SALT HYDROLASE AND DYSLIPIDEMIA: IN VIVO HUMAN STUDY

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Introduction: Serum cholesterol may be regulated by bile acid metabolism in the gut, that depends on bacterial bile salt hydrolase (BSH) activity. There are limiting data regarding the clear effect of BSH on host lipid metabolism.

Aims & Methods: Aim of investigation was to assess the relationship between the gut bacterial BSH relative activity (RA) and lipid profile values. The study included 26 almost healthy participants (control group) and 77 patients with dyslipidemia and without anamnesis of major cardiovascular events. Fecal samples were collected for evaluation of total RA of gut BSH. The new photometric enzyme assay was used for the assessment of total RA of gut BSH. The serum lipid profile values were evaluated using enzymatical methods. For determining the statistical relationships between variables, the correlation and logistic regression analysis were used.

Results: The RA of BSH was higher in healthy adults comparing to participants with dyslipidemia ($p < 0.001$). It was found moderate negative correlation between RA of gut bacterial BSH and total cholesterol (-0.38) and low-density lipoproteins (-0.36). With increasing of RA of gut bacterial BSH, the risk of dyslipidemia decreased ($p < 0.001$), OR = $1.06 \cdot 10^{-10}$ (95% CI; $2.5 \cdot 10^{-15}$ - $4.5 \cdot 10^{-6}$), AUC = 0.845 (95% CI; 0.746-0.943).

Conclusion: The total relative activity of gut bacterial BSH negatively correlated with TC and LDL and was negatively associated with the risk of dyslipidemia.

Disclosure: Nothing to disclose

P1002

POST ERCP-PANCREATITIS IN CORRELATION WITH DIFFERENT TYPES OF MAJOR DUODENAL PAPILLA

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Introduction: Endoscopic papillosphincterotomy (EPT) serves as a cornerstone in the treatment of biliary tract diseases although with a fair share of complications like acute pancreatitis.

Aims & Methods: Our research aims to determine the risk of acute pancreatitis in patients who had undergone EPT in correlation with different types of major duodenal papilla (R.H. Hawes, 2018).

We studied 746 who had undergone successful endoscopic transpapillary intervention (ETI) between 2010 and 2017. They were divided into two groups. Group A consisted of 432 patients (57.9%; age - 51.96 ± 17.6 ; males - 45.83% and females - 51.16%) who had undergone ETI without the use of guidewire and prophylactic stenting of pancreatic duct. Group B consisted of 314 patients (42.1%; age - 52.41 ± 17.6 ; males - 45.54% and females - 54.45%) who underwent ETI with guidewire and prophylactic stenting and drainage of pancreatic duct.

Results: Occurrence of severe form of acute pancreatitis was higher in group A, especially in patients with an accentuated S-shaped papilla, and a "shar-pei" type of papilla. Although serum amylase levels in group B were higher than normal, post-procedural pancreatitis was rarely ob-

served. Group B patients also had reduced incidences of purulent necrotic changes in the pancreas and the retroperitoneal space which was reflected in the decreased number of laparotomies in this regard.

Conclusion: Guidewire usage along with stenting and drainage of the pancreatic duct helps reduce incidences of post-procedural acute pancreatitis especially in patients with S-shaped major duodenal papilla.

Disclosure: Nothing to disclose

P1003

BILIARY LIPID COMPOSITION IN PATIENTS WITH CHOLESTEROL GALLSTONE DISEASE: DIFFERENCES BETWEEN THE GENERAL POPULATION AND PATIENTS AFTER BARIATRIC SURGERY

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Introduction: The pathogenesis of cholesterol gallstone formation is still unclear. Supersaturated bile seems to play an important role, as well as crystallization-promoting factors. We hypothesize that the biliary lipid composition of traditional cholesterol gallstone patients and patients who developed cholesterol gallstones after bariatric surgery differ.

Aims & Methods: Immediately after cholecystectomy, gallbladder bile was obtained from 19 traditional cholesterol gallstone patients, 21 patients who developed cholesterol gallstones after bariatric surgery, 7 patients who already had cholesterol gallstones before they received bariatric surgery but developed symptoms afterwards, and 8 gallstone-free bariatric patients. Biliary lipid composition, cholesterol saturation index (CSI) and cholesterol crystals were analyzed.

Results: Patients who formed gallstones after bariatric surgery had a higher median bile acid (BA) concentration compared to traditional gallstone patients (139.1 vs 89.2 mM; $p=0.039$), higher cholesterol concentration (12.2 vs 6.0 mM; $p=0.001$), higher phospholipid concentration (31.8 vs 18.0 mM; $p=0.061$), higher total biliary lipid concentration (9.6 vs 5.9 g/dL; $p=0.020$), and higher CSI (113 vs 87; $p<0.001$). They had a significant lower BA concentration compared to gallstone-free bariatric patients (139.1 vs 175.5 mM; $p=0.041$), lower total biliary lipid concentration (9.6 vs 11.9 g/dL; $p=0.047$) and higher CSI (113 vs 81; $p=0.002$). Biliary lipid composition and CSI did not differ between bariatric patients who formed gallstones after bariatric surgery and bariatric patients who already had gallstones but developed symptoms afterwards. In all groups, the majority (>85%) of patients had cholesterol crystals.

Conclusion: Our results indicate that gallstone formation follows different trajectories in traditional patients versus morbidly obese patients that have undergone bariatric surgery. In the latter group, cholesterol saturation seems the primary driving factor, whereas in the traditional group non-lipid factors may be more important.

Disclosure: Nothing to disclose

P1004

EFFECT OF POST-ERCP CHOLECYSTECTOMY VS. PRIMARY ERCP ALONE ON THE RATE OF RECURRENT COMMON BILE DUCT STONES

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Introduction: Gallstone diseases have a high prevalence in western populations and pose a large burden to health care systems. While endoscopic retrograde cholangiopancreatography (ERCP) is the primary treatment of choice for common bile duct stones (CBDS), post-ERCP cholecystectomy (CCY) is often performed to prevent recurrent gallstone disease. The effect of post-ERCP CCY compared to primary ERCP alone on the rate of recurrent CBDS has not been described in a general population over a prolonged period of time.

Aims & Methods: Our aim was to investigate the effect of post-ERCP CCY compared to primary ERCP alone on the rate of recurrent CBDS during 5-year follow-up from time of definitive intervention. Using an internal ERCP database at Odense University Hospital, we identified all patients that underwent ERCP for CBDS between January 1 1995 and August 31 2019. Patients with known hepatobiliary or pancreatic malignancies at the time of ERCP were excluded. Patient characteristics, clinical presentation and information on endoscopic procedures were retrieved from the ERCP database. Information on comorbidities, recurrent CBDS and performance of post-ERCP CCY were retrieved from the Danish National Patient Registry (in ICD-10 and SKS codes). The effect of post-ERCP CCY compared to ERCP alone on the rate recurrent CBDS was investigated using logistic regression, with adjustment for confounding covariates.

Results: During the study period 1,768 consecutive patients that underwent ERCP for CBDS fulfilled the inclusion criteria. Among these, 635 patients received post-ERCP CCY (within half a year after primary ERCP) and 1,133 received ERCP alone. Differences between the CCY and no CCY group were observed in age ($p<0.01$) and gender ($p<0.01$). The rate of recurrent CBDS during 1-year follow-up was 16% ($n=104$) for the CCY group and 18% ($n=209$) for the no CCY group ($p=0.30$). During 5-year follow-up the rate of recurrent CBDS was 23% ($n=149$) in the CCY group and 21% ($n=239$) in the no CCY group ($p=0.27$). Neither age or gender were independently associated with risk for recurrent CBDS at 5-year follow-up ($p>0.1$ for both). Performance of CCY was not associated with reduced risk of recurrent CBDS during 5-year follow-up - in both univariate analysis (OR [95% CI]: 1.15 [0.91-1.45]; $p=0.25$) and multivariate analysis (OR [95% CI]: 1.07 [0.82-1.41]; $p=0.61$) after adjustment for age (OR [95% CI]: 1 [0.99-1.00]; $p=0.51$) and comorbidities (Charlson Comorbidity Index, CCI) (OR [95% CI]: 0.52 [0.27-0.97]; $p=0.04$).

Conclusion: Our results indicate that post-ERCP CCY is not associated with reduced rates of recurrent CBDS compared to ERCP alone during a prolonged follow-up period of 5-years from the time of intervention.

Disclosure: Nothing to disclose

P1005

A VALIDATED SCORE PREDICTING COMMON BILE DUCT STONE IN PATIENTS HOSPITALIZED WITH CALCULUS CHOLECYSTITIS: A MULTI-CENTER STUDY

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Introduction: Concomitant common bile duct (CBD) stone in the setting of acute calculous cholecystitis (ACC) should be suspected once abnormal liver indices are noticed.

Aims & Methods: We aimed to identify predictors of CBD stone in patients hospitalized with ACC. We performed a retrospective multicenter case control study from 1st January 2016 till 31st December 2018. Inclusion criteria included patients with an established diagnosis of ACC based on clinical, laboratory and radiological criteria and who had endoscopic ultrasound (EUS) for suspected CBD stone. One-hundred and twelve patients were included, of these fifty-three patients (47.3%) were diagnosed with CBD stone by EUS.

Results: In univariate analysis, Age (OR 1.038, P=0.001), total bilirubin (mg/dl) (OR 1.429, P=0.02) and CBD width (mm) by US (OR 1.314, P=0.01) were statistically significant in predicting CBD stone and remained significant in multivariate regression analysis. We developed a diagnostic score that included these three parameters, with assignment of weights for each variable according to the coefficient estimate.

Each parameter (overall 3 parameters) was given 1 point, so that the overall score is composed from 3 points (scale 0-3). A low cut-off score of 0 was associated with sensitivity of 100% for CBD stone, whereas a high cut-off score of 3 was associated with sensitivity of 10% and specificity of 96.6% with a positive predictive value of 67% (ROC of 0.7558). We validated this score with an independent cohort (ROC of 0.7416) with sensitivity of 46.6%, specificity of 91.5% and PPV of 87.1%.

Conclusion: We recommend incorporating this score as an aid for stratifying patients with ACC into low or high probability for concomitant CBD stone.

Disclosure: Nothing to disclose

P1006

CHOLECYSTECTOMY FOLLOWING ERCP FOR COMMON BILE DUCT STONES (CBDS) - ARE WE GETTING IT RIGHT?

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Introduction: Patients with CBDS undergoing ERCP and duct clearance should have early cholecystectomy (CCY) to minimise the risk of recurrent biliary complications and acute pancreatitis. The British Society of Gastroenterology (BSG) recommends CCY as a definitive management for patients with concomitant gallbladder (GB) and CBDS. For patients with mild acute gallstone pancreatitis, CCY should be performed within 2 weeks of presentation(1).

Recently the European Society of Gastrointestinal Endoscopy (ESGE) recommended CCY within 2 weeks following ERCP in CBDS patients to minimise the risk of recurrent biliary events(2).

Aims & Methods:

- 1) To determine time frame between ERCP and CCY in non-pancreatitis group
 - 2) To determine time frame between ERCP and CCY in pancreatitis group
 - 3) To determine re-admission rate with biliary events whilst awaiting CCY
- All patients who underwent ERCP for CBDS in our centre between 1/7/2018 to 31/7/2019 were included. Patients with prior CCY were excluded. All patients were followed up for at least 6 months following their ERCP.

Results: 216 patients underwent ERCP for CBDS. 47 patients with prior CCY were excluded. 45.6% (77/169) of patients with gallbladder in situ underwent CCY. Median time between ERCP and CCY was 105 days (range 0-379 days). In the CCY group, 10 patients had mild pancreatitis - median time between ERCP and CCY was 54.7 days (range 1 - 169 days). 30% (3/10) of the patients with mild pancreatitis and 10.4% (8/77) of patients overall underwent CCY within 2 weeks of duct clearance.

Table compares the CCY and non-CCY group.

CCY Group (n=77) Non-CCY group (n=92)

Median Age (years) 59 vs 75

Female (%) 65 vs 48

Pancreatitis on presentation (%) 13 vs 9.8

Readmission with recurrent CBDS 3.9 vs 5.4

In the non-CCY group, 52% were deemed unfit for surgery, 15% declined surgery, 13% await appointment for surgery, 15% await surgical outpatient appointment and 5% were not referred for surgery. In the non-CCY group, 9 patients had mild gallstone pancreatitis - 3 were deemed unfit for CCY, 3 await surgical outpatient appointment, one await appointment for CCY, one declined CCY and one patient was not referred for CCY.

Conclusion: The median time between ERCP and CCY was high in our organisation. Only a small proportion of patients in the mild pancreatitis and non-pancreatitis groups underwent CCY within 2 weeks of duct clearance. Local pathways including early referral, prompt surgical assessment of patients deemed fit for surgery and access to regular hot CCY lists should be established to streamline the management of these patients and ensure adherence to the published guidelines.

References: 1. Updated guideline on the management of CBDS: BSG guidelines. Gut 2017 May 2. Endoscopic management of common bile duct stones: ESGE guideline. Endoscopy 2019 Apr 3

Disclosure: Nothing to disclose

P1007

EFFICACY OF DOUBLE-BALLOON ENTEROSCOPY FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY: SPECIALISTS IN DBE AND RENDEZVOUS METHOD WITH PTBD IMPROVE SUCCESS RATE

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Introduction: Recently, the usefulness of the endoscopic retrograde cholangiopancreatography (ERCP) using double-balloon enteroscope (DB-ERCP) has been reported in patients with an altered anatomic intestine, such as Roux-en-Y gastro- or esophago-jejunostomy (R-Y) and hepatico- or choledocho-jejunostomy anastomosis (HJ). However, there have been differences in success rate among authors because of the difficulty of technique and the need for various inputs, such as time, manpower, and usage

of non-designated devices for biliary treatment. We belatedly started DB-ERCPs from 2015 in earnest, and we are dealing with patients with some difficulty and ingenuity. The aim of this study was to evaluate the efficacy and safety of DB-ERCP at our institute.

Aims & Methods: Sixty-three patients (147 procedures) with R-Y or HJ underwent DB-ERCP at our hospital between April 2015 and March 2020. The procedures were performed with the EI 530 or 580BT (Fujinon, Osaka, Japan). Scope insertion to the papilla of Vater or bilioenteric anastomosis were treated with by a physician specializing in DBE from 2015 to 2018 (Period A), and a physician specializing in ERCP (not DBE) from 2019 to 2020 (Period B). In both periods, pancreato-biliary procedures were done by a physician specializing in ERCP. We retrospectively analyzed the success rate of reaching the objective site, bile or pancreatic duct cannulation, therapeutic procedure, and DBE-related complications.

Results: Sixty-three patients (median age of 73.5 (29-89) years) were comprised of 49 males and 17 females. There were 40 patients (80 procedures) with R-Y and 23 patients (61 procedures) with HJ. Objective site was reached in 67/80 procedures (83.8%) in a median duration of 24.2 min (5- 71) min in R-Y and 54/61 procedures (88.5 %), 29.6 (6-83) min in HJ. Bile duct or pancreatic duct cannulation was successful in 53/67 procedures (79.1 %) in R-Y and 49/55 procedures (89.1 %) in HJ. This result was relatively fair. DB-ERCP related complications occurred in two procedures (2/147, 1.4 %) including intestinal perforation due to scope and pancreatic duct penetration due to pancreatic duct cannulation.

In 40 patients in R-Y, the indication of DB-ERCP was choledocholithiasis (n=21), bile duct stricture (n=12), and other (n=7). Therapeutic interventions using only DB-ERCP were successful in 28/40 (70.0%). Four patients in unsuccessful cases achieved endoscopic success using a rendezvous method with percutaneous transhepatic biliary drainage (PTBD). Overall success rate was 80% (32/40).

The success rate of reaching to the papilla of Vater was better in group A than group B (A: 33/34,97.1%, B:34/46, 73.9%) and the success rate of bile duct cannulation was equivalent (A: 26/33, 78.8%, B:27/34, 79.4%). In comparison, the success rate of reaching the bilioenteric anastomosis and bile duct cannulation was not different between A (22/24, 91.6 %,21/22,95.5%) and B (33/38,86.8 %,28/33, 84.8%).

Conclusion: Diagnostic and therapeutic DB-ERCP are relatively safe and effective in patients with altered gastrointestinal anatomy. There were some difficult cases, especially in R-Y gastro- and esophago-jejunostomy. Considering the results in this study, scope insertion by a specialist in DBE and the rendezvous method using PTBD might improve the success rate of scope insertion, bile duct cannulation, and overall therapeutic procedure.

Disclosure: Nothing to disclose

P1008

FUNCTIONAL DYSPEPSIA AND IRRITABLE BOWEL SYNDROME NEGATIVELY AFFECT PATIENT REPORTED OUTCOMES AFTER CHOLECYSTECTOMY: A PROSPECTIVE, MULTICENTRE, OBSERVATIONAL STUDY (PERFECT - TRIAL)

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Introduction: More than 40% of patients with symptomatic gallstone disease reports persisting pain following cholecystectomy. Co-existence of functional dyspepsia (FD) and irritable bowel syndrome (IBS) may contribute to this unsatisfying outcome.

Aims & Methods: We aimed to determine the prevalence of FD and IBS in patients eligible for cholecystectomy and to investigate the influence of FD/IBS on the resolution of biliary colic and a pain-free state.

We conducted a multicentre, prospective, observational study (PERFECT-trial). Patients, ≥18 years with uncomplicated cholecystolithiasis were included from five surgical outpatient clinics, between January 2018 and April 2019. Follow-up was continued for six months. The primary outcome was the prevalence of FD/IBS, assessed with the validated ROME-IV questionnaire. Biliary colic was defined by the ROME-criteria. Pain-free was defined as Izbicik Pain Score ≤10 and a visual analogue scale ≤4.

Results: We included 401 patients (52 years, 76% females), 34.9% (140/401) fulfilled the ROME-IV criteria for FD/IBS, and 64.1% (257/401) fulfilled the ROME criteria for biliary colic. Thirty patients were lost to follow-up. In total, 74.9% of patients (278/371) underwent cholecystectomy. The cholecystectomy-rate was similar in the FD/IBS-group compared to the group without FD/IBS (73.8% vs. 75.5% respectively, p=0.72). After cholecystectomy, 6.1% of patients fulfilled criteria for biliary colic (4.9% in FD/IBS patients vs. 8.6% in patients without FD/IBS, p=0.22) A pain-free state was achieved in 56.8% of patients who underwent cholecystectomy, 40.7% in FD/IBS-group vs. 64.4% in patients without FD/IBS, p< 0.001.

Conclusion: One-third of patients eligible for cholecystectomy fulfil criteria for FD/IBS. After surgery, only a few patients report biliary pain, but non-biliary abdominal pain persists in almost half of the patients, particularly in those with FD/IBS pre-cholecystectomy. FD and IBS are major risk factors for persistent abdominal pain. Clinicians should take these symptom-dependent outcomes into account in their shared decision making process.

Disclosure: Nothing to disclose

P1009

VERIFICATION OF THE EFFECT OF NEAR INFRARED PHOTOIMMUNOTHERAPY (NIR-PIT) ON CHOLANGIOCARCINOMA AND AVAILABILITY OF THE NOVEL CATHETER DEVICE WITH LIGHT EMITTING DIODES (LEDs) IN VIVO

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Introduction: As cholangiocarcinoma (CCA) is difficult to treat, surgical resection and chemotherapies are mainly performed in clinical practice. Near infrared photoimmunotherapy (NIR-PIT) is a novel therapy for cancers with NIR light and monoclonal antibody photosensitizer conjugates. An international phase III clinical trial of NIR-PIT is now ongoing for patients who have recurrent head/neck cancer. While, NIR-PIT has a limitation to be performed in CCA. It is difficult to deliver NIR light into the deep regions such as the bile duct from the extracorporeal apparatus because the light is absorbed by surrounded normal tissues.

Thus, we developed a dedicated catheter device with LEDs which can be inserted into the bile duct and evaluated the effect of antibody-IR700 conjugates on CCA cell lines and the NIR-PIT with the new device in vivo.

Aims & Methods: The aim of this study is to verify the NIR-PIT efficacy for CCA in vitro and validate the effect with the new device in vivo. Human CCA cell lines: HuCCT-1, YSCC, TFK-1, and KMCH-1 were used for this study. In in vitro experiment, we measured EGFR or HER2 expression on these cell lines using fluorescence microscopy and flow cytometry assay. In addition, we performed NIR-PIT on HuCCT-1 and YSCC using the panitumumab (anti-EGFR antibody)-IR700 conjugates. TFK-1 and KMCH-1 were also performed using the trastuzumab (anti-HER2 antibody)-IR700 conjugates. Thereafter we evaluated its efficacy on flow cytometry assay. In in vivo experiment, mice were subcutaneously inoculated with HuCCT-1 cells and the newly developed catheter was implanted under the tumor. Mice were divided into 6 groups (1) IR700 (+), catheter (+), NIR (+), (2) IR700 (+), catheter (+), NIR (-), (3) IR700 (+), catheter (-), NIR (-), (4) IR700 (-), catheter (+), NIR (+), (5) IR700 (-), catheter (+), NIR (-), and (6) IR700 (-), catheter (-), NIR (-). IR700 (+) mice were injected with panitumumab-IR700 conjugates intravenously. NIR (+) mice were irradiated by the catheter one day after the injection of panitumumab-IR700 conjugates. Mice were observed for two weeks to evaluate the tumor size and body weight. Moreover, histological analysis was performed after NIR-PIT.

Results: EGFR expression on HuCCT-1 and YSCC cells was confirmed by microscopy and flow cytometry. HER2 expression on KMCH-1 was also confirmed, but TFK-1 did not express HER2. The cell death of these cells confirmed target expressions, was significantly found after NIR-PIT on flow cytometry assay ($p < 0.001$). The number of dead cells was increased dose-dependently by NIR-light radiation. In in vivo studies, the tumor growth in the group (1) using the new catheter was significantly suppressed ($p < 0.001$). In the group (2), (3), (4), and (5), the tumor growth was similar to that of the group (6). There was no difference in body weight before and after treatment in all groups. In histological analysis, H&E staining of tumors after NIR-PIT revealed the cell death, while no damage was observed in untreated tumors.

Conclusion: NIR-PIT for the CCA cells that express EGFR or HER2 is effective and the novel catheter device with LEDs is feasible and available to perform NIR-PIT. For further studies, allograft models are necessary to identify the therapeutic effect of NIR-PIT including immunogenic cell death.

Disclosure: Hirata H and Kuwatani M. received funding from Japan Lifeline Co., Ltd. for this study. The funder was not involved in the study design, analysis and interpretation of the data.

P1010

GALLBLADDER NEUROENDOCRINE CARCINOMAS ARISING IN A BACKGROUND OF BILIARY INTRAEPITHELIAL NEOPLASIA AND INTRACHOLECYSTIC PAPILLARY NEOPLASM SUGGEST MONOCLONAL ORIGIN

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Introduction: Gallbladder (GB) neuroendocrine carcinomas (NECs) and mixed neuroendocrine non-neuroendocrine neoplasms (MiNENs) are rare and highly aggressive entities. The cell of origin of GB NECs and MiNENs has been matter of controversy, leading to two hypotheses that both have been poorly investigated: either NEC cells develop from pre-existing neuroendocrine cells and may grow together with an AC (precursor), or AC cells undergo lineage transformation into NEC cells.

Aims & Methods: Here, we performed a comparative histopathological and molecular analysis of GB NEC/MiNEN cases and associated intracholecystic papillary neoplasm (ICPN) and biliary intraepithelial neoplasia (BilIN) precursor lesions. Cases without a precursor lesion were included as well for molecular comparison with those arising in the background of a precursor. We selected cases diagnosed between 2000 and 2019 by combining databases of the Netherlands Cancer Registry and the nationwide network and registry of histo- and cytopathology in The Netherlands (PALGA). Precursors and carcinomas were immunohistochemically compared and analysed for microsatellite instability (MSI), tumour mutational burden (TMB) and mutations and gene amplifications in 523 cancer-related genes.

Results: Ten neuroendocrine cases (90% female) were identified, with a median age of 67.5 years (range: 42-79). Sixty percent of cases showed a precursor lesion, either ICPN (three cases) or BilIN (three cases). In 90% of cases, at least one tumor component (either NEC or, if present, AC) showed angioinvasion; lymphatic invasion and perineural invasion were observed in 70% and 20% of cases, respectively. Neuroendocrine expression (with synaptophysin, chromogranin A and CD56) confirmed neuroendocrine histology and was absent in the precursor lesions. ICPNs were all positive for CK7 and two out of three were also positive for CK20, whereas corresponding NEC components were negative. Preliminary results of molecular profiling were obtained for three NECs (will be increased to 10 cases). These cases revealed (likely) pathogenic mutations in *TP53* (all cases), *RB1* (2/3 cases) and *PIK3R1* (one case), that were shared in all three cases between precursor and invasive carcinoma. Two out of three cases were microsatellite stable (both components) and their median non-synonymous TMB was 2.8 mutations/Mb. One case did not meet the quality control for MSI and TMB analysis.

Conclusion: Our data provide insight into the development of GB NECs and suggest monoclonal origin of different epithelial precursor lesions and invasive neuroendocrine components, favouring the hypothesis of lineage transformation.

Disclosure: Nothing to disclose

P1011

RELATION BETWEEN *HELICOBACTER SPP.* ISOLATED IN BILE AND BILIARY TRACT MALIGNANCIES

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Introduction: The increased incidence of neoplastic lesions of the biliary tract, as well as their high mortality, require measures to detect factors associated with their development. *Helicobacter spp.* has been related to this type of cancer, however, there are big differences in the results, according to geographic factors and the methods used for the detection. *Helicobacter* isolation has been performed in bile tissue or bile from intra-operative samples. Demonstrating the association of this pathogen in bile would represent an advance in the prevention and knowledge of these malignancies.

Aims: To compare the proportion of *Helicobacter spp.* in bile of patients with malignant or benign biliary obstruction. To analyze the association between the bacteria and bile tract cancer. To describe the baseline characteristics, laboratory values, and comorbidities of these patients, as well as characteristics related to ERCP procedure and its complications.

Methods: Cases and controls prospective study. We included 98 patients admitted between April and November 2019, who underwent a bile drainage procedure by ERCP. Samples of bile were obtained, after biliary cannulation, with the sphincterotome. *Helicobacter* detection was carried out by polymerase chain reaction. Variables related to demographic data, comorbidities, hospital stay and ERCP procedure were collected. Descriptive statistical calculation of the variables of interest, differentiating between the presence of malignancy or not was performed. We analyzed the data with SPSS using Chi-square test for qualitative variables and Mann-Whitney test.

Results: We studied 55 men and 43 women, who underwent ERCP due to bile duct pathology. Average age 72.7 (28-94) years. Median time from diagnosis of biliary pathology to admission, 13 days, and from admission to ERCP 1 day. The reason for ERCP was 73.5% choledocholithiasis, 19.4% malignant obstructive jaundice (47.4% pancreatic origin, 31.4% cholangiocarcinoma, 10.3% ampuloma, 10.3% malignant extrinsic compression of other origin), 6.1% benign stenosis, 1% biliary fistula. 23.5% had undergone an ERCP before. 15.3% had biliary stent previously placed and 28.6% required placement of a biliary stent for the first time. Post-ERCP complications: 1% pancreatitis and 2% hemorrhage. Average hospital stay 5.5 days. Global detection of *Helicobacter spp.* in bile samples 17.3%, with 94.2% of them being *H. Pylori*. *Helicobacter* was isolated in 17.7% of the malignant lesions.

We did not find an association between *Helicobacter* in bile and neoplasia $p > 0.05$. On the other hand, there is a statistically significant association between neoplasia and diabetes $p = 0.006$, absence of cholecystectomy $p = 0.015$, prothrombin activity value $p = 0.0001$, bilirubin value at admission $p = 0.0001$ and hemoglobin value at admission $p = 0.02$.

Conclusion: A significant percentage of *Helicobacter spp.* have been detected in bile. We did not find association between *Helicobacter spp.* and bile tract malignancies, although the small sample size could be related to the lack of association obtained. We have found an association between analytical alterations on admission and neoplasia, as well as the presence of diabetes and the absence of cholecystectomy.

Disclosure: Nothing to disclose

P1012 WITHDRAWN

P1013

EFFECTIVENESS OF BILE CYTOLOGY USING ENDOSCOPIC TRANSPAPILLARY GALLBLADDER DRAINAGE TO DISTINGUISH GALLBLADDER CANCERS FROM BENIGN GALLBLADDER DISEASES - A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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Introduction: It is often difficult to distinguish gallbladder carcinoma from benign gallbladder diseases. Some investigators have reported diagnostic accuracy of gallbladder disease using endoscopic transpapillary gallbladder drainage (ETGD). However, these results have been obtained retrospectively. Therefore, we conducted a prospective, clinical trial to evaluate the diagnostic accuracy of cytology from ETGD in gallbladder disease.

Aims & Methods: A total of 35 consecutive patients who scheduled to undergo ETGD from March 2017 through September 2019 were prospectively enrolled. ETGD was applied to gallbladder diseases which were difficult to diagnose benign or malignant by radiological findings. Patients were inserting 5F pigtail nasobiliary drainage tube in Gallbladder and cytology samples were collected over five times using liquid-based cytology. If ETGD failed, a 5Fr drainage tube was placed into the bile duct. The primary endpoint was diagnostic accuracy of ETGD cytology, and secondly endpoint were technical success rate, adverse events.

Results: Selective bile duct cannulation was success in all patients. Among them, success rate of inserting ETGD tube was 85.7% (30/35), including 16 of 19 patients with GBC (84.2%) and 14 of 16 with benign gallbladder diseases (87.5%). Total procedure time was 43 (15-108) min. Type 2 cystic duct pattern (angle down and located on the right side) was the independent risk factor for ETGD failure (OR13.5; 95%CI 1.7-143.7; $p=0.02$). Cytology was conducted 5 times on median (range, 3-7).

Sensitivity, specificity, and accuracy in all patients were 78.9%, 100%, and 88.6%, respectively. Those in the 30 patients with successful ETGD were 87.5%, 100%, and 93.3%, respectively. In contrast, cytology with ETBD tube who failed ETGD tube insertion had 33.3% sensitivity, 100% specificity and 50% accuracy. There was statistical significance in the accuracy of ETGD cytology and ETBD cytology ($p=0.048$).

Adverse events occurred in 3 patients (8.6%), including mild post-ERCP pancreatitis in 1 (2.9%) and obstructive jaundice in 2 (5.8%), and all complications were resolved with conservative therapy.

Conclusion: Cytology using an ETGD tube is useful in the diagnosis of gallbladder diseases, for which it is difficult to distinguish between benign and malignant lesions.

Disclosure: Nothing to disclose

P1014 WITHDRAWN

P1015

USEFULNESS OF A NEWLY DESIGNED HEMOCLIP IN ENDOSCOPIC AMPULLECTOMY: A RETROSPECTIVE STUDY

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Introduction: Endoscopic ampullectomy for duodenal ampullary adenoma has become a safe and efficacious treatment which could avoid the need for invasive open surgery. However, serious adverse events such as massive bleeding, post ampullectomy pancreatitis or perforation is the clinical problems. There are a few reports on a suitable additional procedure for prevention of adverse events during endoscopic ampullectomy.

Aims & Methods: Therefore, we evaluated new rotatable hemoclip that can be easily handled even when it is bent strongly through a side-viewing endoscope. This retrospective study was conducted from 2014 to 2020. Patients with pathologically proven ampullary adenoma who underwent endoscopic papillectomy were enrolled. The efficacy and feasibility of newly developed hemoclip (Sure clip, MicroTech, Nanjing, China) were evaluated.

Results: We reviewed 56 consecutive patients who underwent endoscopic ampullectomy. After endoscopic snare ampullectomy and subsequent pancreatic stent placement, we tried to completely close the ulcer lesion using hemoclips. We compared the clinical results of patients using the new designed hemoclip (n = 18) and those using the conventional hemoclip (n = 36). The median number of clips is similar between two groups (new clip group n=3.3±1.6, conventional group n=3.2±1.7). The time required to perform ulcer closure using the new clip was significantly reduced compared to using the conventional clip (5.4±2.7min vs 10.9±8.8min, p=0.014). The rate of complete closure (Odds ratio 144.5, 95%CI 14.9-1394.9, p< 0.01), and the need for hemostatic treatment during ampullectomy (Odds ratio 0.104 95%CI 0.025-0.426, p< 0.01) were significantly more effective in the new clip group compared to the conventional clip group. There was no difference in treatment outcome or adverse events between the two groups.

Conclusion: New designed hemoclip is easy to use and effective for ulcer closure after endoscopic ampullectomy.

Disclosure: Nothing to disclose

P1016

COMPARISON OF STENT'S PATENCY AND PATIENTS' SURVIVAL BETWEEN METAL STENTS PLACEMENT ALONE AND METAL STENTS PLACEMENT AFTER ENDOBILIARY RADIOFREQUENCY ABLATION IN UNRESECTABLE MALIGNANT HILAR OBSTRUCTION

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Introduction: Recently, endobiliary radiofrequency ablation (RFA) has been used as a palliative treatment method for the unresectable malignant hilar obstruction (MHO). Endobiliary RFA with stent placement may help improving stent's patency and patients' survival in MHO. However, there's little study on the role of endobiliary RFA for MHO.

Aims & Methods: This study aimed to find out the efficacy of endobiliary RFA for MHO. We compared the stent's patency and patients' survival between metal stents placement alone group and endobiliary RFA with stents placement group in patients with MHO. The data of consecutive 79 patients (median age: 66 years, male: 51.9 %) between April 2016 and January 2020 were retrospectively analyzed.

Results: The 51 patients (64.6 %) were taken metal stents placement alone (stent alone group), and 28 patients (35.4 %) were taken metal stents placement after RFA (RFA-stent group). All procedures were successful (100 %). During the follow-up periods, stent occlusion occurred in 59 patients (74.7 %), of which 40 patients (78.4 %) were stent alone group, and 19 (67.9 %) were RFA-stent group. In Kaplan-Meier estimates, the stent's patency was 264.9 days in the stent alone group (95% confidence interval (CI), 190.1-339.7) and 180.8 days in RFA-stent group (95% CI, 127.3- 234.3), and there was no statistically difference (P=0.414). Post-procedure survival was 415.9 days in the stent alone group (95% CI, 324.5- 507.3) and 465.5 days in the RFA-stent group (95% CI, 304.4- 626.5), and there was no statistically difference (P=0.938). In the multivariate cox regression analysis, patients who did not receive chemotherapy showed increased risk of stent occlusion compared to those who received chemotherapy (hazard ratio (HR), 2.892 (1.579- 5.294), P=0.001). Endobiliary RFA did not show a significant effect on stent occlusion (HR, 1.150 (0.644- 2.053), P=0.636).

Conclusion: Treatment with metal stents placement after endobiliary RFA in MHO was not associated with improving stent's patency or patients' survival rates. A further prospective randomized study needs to prove the effectiveness of the endobiliary RFA with stents in MHO.

Disclosure: Nothing to disclose

P1017

CLINICAL OUTCOMES OF PATIENTS WITH HILAR CHOLANGIOCARCINOMA UNDERGOING PREOPERATIVE RIGHT PORTAL VEIN EMBOLIZATION

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Introduction: Preoperative portal vein embolization (PVE) has been used to induce hypertrophy of the future liver remnant. However, clinical outcomes of patients with hilar cholangiocarcinoma undergoing preoperative PVE remain uncertain.

Aims & Methods: Fifty-three patients with hilar cholangiocarcinoma who underwent preoperative right portal vein embolization before major hepatectomy from January 2006 to February 2020 were retrospectively reviewed. Patients were stratified into two groups according to the 30-day interval from PVE to operation. Clinicopathologic characteristics and survival outcomes were compared between the two groups.

Results: Among 53 patients, there was no severe PVE-related complication, but 6 patients failed to proceed to surgery because of insufficient increase in liver volume, insufficient biliary drainage, or tumor progression. Among 47 patients who underwent curative-intent surgery, R2 and R1 resection occurred in 8 (17.0%) and 12 (25.5%) patients, respectively. In 38 patients undergoing radical resection including R0 and R1 resection, Bismuth type IV was in 23 (59.0%) patients and extended right hemihepatectomy was performed in 36 (94.7%) patients.

Moderate/poor differentiation was in 29 (76.3%) patients, pT3/pT4 in 6 (15.8%) patients and pN1/pN2 in 18 (47.4%) patients. Major complication (Clavien-Dindo ≥III) occurred in 20 (52.6%) patients including in-hospital mortality of 6 (15.8%) patients. Median length of hospital stay after sur-

gery was 20 days. Median interval of PVE to operation was 30 days. When stratified according to the 30-day interval of PVE to operation, two groups did not differ in terms of sex, age, Bismuth type, operation type, tumor size, histologic differentiation, pathologic TNM staging and status of resection margin.

Between the two groups, there was no significant difference in major complication (50.0% vs 55.0%; $P = 1.00$), in-hospital mortality (16.7% vs 15.0%; $P = 1.00$), median length of hospital stay (20 days vs 20 days; $P = 0.64$) and median RFS (14.9 months vs 7.6 months; $P = 0.20$), and median OS (26.5 months vs 15.9 months; $P = 0.40$).

Conclusion: A quarter of patients failed to receive curative resection after portal vein embolization. Further studies are required to identify subset of patients who would benefit from preoperative PVE and subsequent surgical resection.

Disclosure: Nothing to disclose

P1018

TO EVALUATE THE ROLE OF DIGITAL CHOLANGIOSCOPY USING SPYGLASS OVER THE RESECTABILITY OF PERIHILAR CHOLANGIOCARCINOMA

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Introduction: To precisely assess the disease extent and resectability of perihilar cholangiocarcinoma is still challenging. Bismuth-Corlette classification is so far the most widely used system for assessment of resectability of prehililar cholangiocarcinoma. Magnetic resonance image(MRI) combined with magnetic resonance cholangiopancreatography (MRCP) is regarded as an excellent tool for evaluation the extent of disease, however about 20 percent of cases is still understaged by MRCP.

Aims & Methods: We tried to use digital cholangioscopy with Spyglass (Boston Scientific, Natick, Massachusetts, USA) to localize perihilar cholangiocarcinoma more precisely to guide further surgical strategy. From June 2015 to December 2020, the patients who underwent digital cholangioscopy with Spyglass in Far Eastern Memorial Hospital for evaluating perihilar cholangiocarcinoma were retrospectively enrolled. The accuracy of evaluating extent of disease according to Bismuth-Corlette classification by cholangioscopy with Spyglass was compared with the image study before Spyglass by using surgical pathologic diagnosis as gold standard.

Results: There were 36 patients who underwent cholangioscopy with Spyglass in Far Eastern Memorial Hospital during study period. Among them, 4 patients with suspected perihilar cholangiocarcinoma who received cholangioscopy with Spyglass and had final surgical pathological diagnosis were enrolled. They were all male with a mean age of a 55.5 years (range, 35 to 79 years). All of them underwent contrast enhanced computed tomography (CT), and one case also received MRI/MRCP study before cholangioscopy with Spyglass. Using cholangioscopy with Spyglass for determining the extent of disease showed 100% accuracy by using surgical pathologic diagnosis as gold standard with two cases showing Bismuth-Corlette classification type 4, one case showing type 3A, and one case showing type 3B, while contrast enhanced CT showed only 25% accuracy. One case was changed from intentional extended left hepatectomy to extended right hepatectomy due to one skipped cancerous looking like

lesion found in posterior branch of right intrahepatic duct, while the other three cases were remained in original surgical plan of extended left hepatectomy.

Conclusion: We demonstrated the excellent performance of cholangioscopy with Spyglass for evaluating tumor extent of perihilar cholangiocarcinoma, and it may change surgical plan according to the findings. Further study is warranted to demonstrate its application on localization of perihilar cholangiocarcinoma for providing precise treatment.

Disclosure: Nothing to disclose

P1019 WITHDRAWN

P1020

SIGNIFICANCE OF *IN VITRO* PHOTODYNAMIC CYTODIAGNOSIS BY GIVING 5-AMINOLEVULINIC ACID FOR MALIGNANT BILIARY STRICTURE

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Introduction: Early detection and diagnosis are important for improving the prognosis of biliary-pancreatic carcinoma. For the diagnosis of malignant biliary stricture, the conventional bile duct smear cytology (conventional method) with endoscopic retrograde cholangiopancreatography (ERCP) is not enough sensitive, and it is necessary to increase the sensitivity for early diagnosis. Recently photodynamic diagnosis (PDD) by oral administration 5-aminolevulinic acid (5-ALA) has been gaining attention to diagnosis of neoplastic diseases in the field of urology and neurosurgery.

We had already reported *in vitro* method of photodynamic cytodagnosis (PDCD) using the reagent 5-ALA for pancreatic carcinoma (1). In the present study, *in vitro* method of PDCD using the reagent 5-ALA for malignant biliary stricture was investigated and the accuracy of PDCD was assessed.

Aims & Methods: Bile duct smear cytology with ERCP was performed for patients with biliary stricture who were admitted to Osaka Rosai Hospital from September 2015 to December 2019. Cells were obtained by bile duct smear and divided into two parts. Some cells were placed on a slide glass for cytodagnosis (conventional method), while other cells were placed in a culture fluid for use in PDCD. ALA is the natural precursor in the heme biosynthetic pathway that induces the intracellular accumulation of endogenous protoporphyrin IX (PPIX) when provided exogenously in large excess. It is characterized by excessive intracellular accumulation in cancer cells. Samples were diagnosed independently by conventional method and PDCD. The definitive diagnosis of benign or malignant diseases was evaluated with the histopathological examinations on surgical specimens. In patients who did not undergo surgery, the final diagnosis was evaluated with the clinical, radiological, and serological evaluation during follow-up over 6 month as well as the histopathological examinations on biopsy of biliary stricture.

Results: One-hundred seventy patients with biliary stricture (92 males and 78 females, average age: 73.6 years old [37-93 years old]) were enrolled in this study. The definitive diagnosis were 35 benign and 135 malignant disease. When we regard Class 4 and 5 as malignancy, the conventional method had a sensitivity of 78.5% (106/135), a specificity of 100% (35/35). PDCD showed a sensitivity of 74.8% (101/135) and a specificity of 68.6% (24/35). The conventional method judged 24 malignant lesions as false-negative, but the PDCD method made it possible to successfully

diagnose as malignancy, in 14 among 24 patients. If we can add PDCD to the conventional method, the sensitivity significantly increased to 88.9% (120/135). Focusing on a biliary-pancreatic carcinoma without HCC and lymph nodes swelling (n=126), the sensitivity in the conventional method would be 80.2% (101/126). If we add PTCd to the conventional method, the sensitivity could be 90.5% (114/126), which is significantly higher than that of the conventional method alone (P=0.02).

Conclusion: By *in vitro* PDCD with the 5-ALA, we can effectively and safely diagnose malignant biliary stricture without an expert pathologist. The sensitivity could increase in the diagnosis of malignant biliary stricture by combining PDCD with the conventional method.

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Disclosure: Nothing to disclose

P1021 WITHDRAWN

P1022

LOCALLY ADVANCED INTRAHEPATIC, PERIHILAR AND MID-CHOLANGIOCARCINOMA AND GEMCITABINE/CISPLATIN AS POTENTIAL INDUCTION THERAPY: A RETROSPECTIVE COHORT STUDY

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Introduction: Biliary tract cancer (BTC) comprises around three percent of all gastrointestinal malignancies and can be divided into three groups based on anatomic location; perihilar (pCCA), intrahepatic (iCCA) and distal (dCCA) cholangiocarcinoma. Currently, surgical resection is still the only potentially curative treatment for these patients, but only 20% of the patients qualify for resection because of locally advanced or metastatic disease at presentation. Patients who do not qualify for resection are normally treated with palliative chemotherapy (Gemcitabine (Gem)/ Cisplatin (Cis)).

Aims & Methods: With this retrospective cohort study we aim to explore the potential of Gem/Cis chemotherapy as induction therapy for patients with unresectable locally advanced or borderline resectable intrahepatic (iCCA), perihilar (pCCA) and mid-cholangiocarcinoma (midCCA) resulting in a possible increased exploration rate.

For this study we included patients with iCCA, pCCA and midCCA presented to the Amsterdam UMC in the period between January 2016 and October 2019. For these patients we have collected data to assess the radiological response after three or six cycles of Gem/Cis chemotherapy and the possibility for exploration.

Results: A total of 364 patients with iCCA, pCCA and midCCA were included, 276 patients were qualified as unresectable, of which 65 had locally advanced or borderline resectable non-metastatic disease. Of these, 28 patients were treated with palliative chemotherapy of which 25 patients received more than three cycles. For these patients the radiological response was evaluated, resulting in 22 patients with stable or partial response on the received chemotherapy. Based on surgical and radiological re-evaluations, exploration could have been re-considered in 8 out of 28 patients (28.6%). Four patients underwent re-exploration of whom two patients received radical resection.

Conclusion: Gem/Cis appears to be a feasible induction therapy for initially unresectable locally advanced or borderline resectable iCCA, pCCA and midCCA. The potentially increased exploration and resection rate could lead to improved survival. Based on these results, a prospective trial is needed to further investigate this effect.

Disclosure: Nothing to disclose

P1023

THE EFFICACY AND SAFETY OF ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE BIOPSY IN THE GALLBLADDER MASSES

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Introduction: Endoscopic ultrasound-guided fine-needle biopsy is a widely used modality for acquiring various target samples, but its efficiency in gallbladder masses is unknown.

Aims & Methods: The aim of this study was to estimate the efficacy and safety of endoscopic ultrasound-guided fine-needle biopsy in the evaluation of patients with gallbladder masses. This was a retrospective study. From March 2015 and July 2019, patients who needed to identify the nature of the gallbladder mass through EUS-FNB were included. We performed the technique with a 22 gauge needle on these patients. The outcomes of this study were the adequacy of specimens, diagnosis yields, technical feasibility, and adverse events of the endoscopic ultrasound-guided fine-needle biopsy in gallbladder masses.

Results: A total of 27 consecutive patients with a median age of 58 years (interquartile range [IQR], 52-70) were included in this study. The 22 gauge FNB needle was feasible in all lesions. The median follow-up period of the patients was 217 days (IQR: 85.5-358). The specimens sufficient for diagnosis account for 92.59% and 96.3% in cytology and histology, respectively. The overall diagnostic yield for malignancy showed the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 95.45%, 100%, 100%, 83.33%, and 96.3%, respectively. There was one patient experienced mild abdominal pain after the procedure and recovered within one day.

Conclusion: Endoscopic ultrasound-guided fine-needle biopsy is a reasonable alternative for preoperative diagnosis of unresectable patients before chemotherapy and surgical patients before operation. Further large-scale studies are needed to confirm our conclusion.

Disclosure: Nothing to disclose

P1024

THE CHALLENGE OF OUTRULING CONCOMITANT CHOLANGIOCARCINOMA IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS WAIT-LISTED FOR LIVER TRANSPLANTATION: THE IRISH NATIONAL EXPERIENCE

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic liver disease characterized by a progressive cholestasis due to bile duct inflammation and fibrosis. The condition may lead to end stage liver disease requiring transplantation. Patients are also at risk of developing cholan-

giocarcinoma (CCA). The presence of widespread intra- and extra-hepatic biliary tree stricturing makes the diagnosis of early CCA difficult in patients with advanced PSC. To date there remain no internationally accepted guidelines on CCA surveillance in PSC patients wait-listed for liver transplantation.

Aims & Methods: The purpose of this study was to critically evaluate the Irish Liver Transplant Unit's 12-year experience with the evaluation of wait-listed PSC patients, focusing on diagnostic evaluation, waitlist surveillance and clinical outcomes.

All PSC patients waitlisted for transplant after January 2007 were included. Those with hilar CCA pursuing the Mayo protocol were excluded. Patient demographics and surveillance investigations (modality and frequency) were analysed. Explant pathology was deemed gold standard in diagnosing CCA. Sensitivity, specificity, positive and negative predictive values with exact binomial 95% confidence intervals were calculated. Additional information provided by including multiple tests was calculated using the area under the receiver operating characteristic curve.

Results: Of 77 waitlisted PSC patients, 68 proceeded to transplantation, 5 developed malignancy while waitlisted. Explant liver histology confirmed 51 patients (75%) to have isolated PSC. 6(8.8%) had an incidental finding of either concomitant cholangiocarcinoma or high grade dysplasia on explant histology.

	Patient, n	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CT	77	42.9	68.6	12	92.3
MRI	77	28.6	67.1	8	90.4
PET	7	NA	85.7	NA	100
Brush Cytology	27	66.7	92.3	50	96
FNA	7	50	100	100	83.3
CA 19-9 (>129 U/ml)	77	42.9	78.6	16.7	93.2

[Table I. Accuracy of diagnostic modalities in diagnosing CCA in patients with PSC.]

Conclusion: The approach to investigating this cohort is heterogenous and individualised. HGD and overt malignancy, while infrequent, were still present despite rigorous workup. A structured intensive diagnostic approach is justified.

Disclosure: Nothing to disclose

P1025

UNMET NEEDS IN THE DIAGNOSIS AND TREATMENT OF ROMANIAN PATIENTS WITH BILIO-PANCREATIC TUMORS: RESULTS OF A PROSPECTIVE OBSERVATIONAL MULTICENTRIC STUDY

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Introduction: Biliopancreatic malignancies are among the most aggressive solid neoplasms, and incidence is rising worldwide. Patients with cancers of these organs have extremely poor 5-year survival rates, below 10%. Good patient outcome relies heavily on a multidisciplinary approach to therapy, including timely access to surgery, chemo/radiotherapy and

endoscopic therapy. In our study, we aimed to evaluate current practices as reflected in the management and outcome of patients diagnosed with biliopancreatic tumors (BPT) in the setting of a low-resource medical system in order to identify areas suitable for improvement.

Aims & Methods: We conducted a prospective observational multicentric study including all patients with pancreatic cancers and extrahepatic cholangiocarcinomas evaluated in the participating centers. We collected data on the pathology of the tumors, staging at diagnosis (using computed tomography, magnetic resonance imaging, endoscopic ultrasound), ECOG status (Eastern Cooperative Oncology Group Status), surgical interventions, chemo/radiotherapy and endoscopic drainage where applicable. Telephone follow-up (FU) visits were performed at 3 months after the enrollment visit and additional data was collected regarding subsequent treatment, performance status of the patient, disease-related events and outcomes such as surgery and palliative interventions. Patients who failed to return for planned hospital visits or could not be reached by telephone, were declared lost to follow-up. Data was collected using a standard form and analyzed using SPSS.

Results: Among our patients, the most frequent tumor location was the pancreas (72,1%) and most of the patients presented with advanced disease (42,4% were stage IV at enrollment), despite the favorable ECOG status at presentation (43,6% ECOG 0 at diagnosis). We identified the following unmet needs in the current practices of oncological treatment for patients with biliopancreatic tumors in our cohort: a very low percentage of resectable lesions (only 18% of the patients were operated with curative intent), suboptimal endoscopic palliative treatment (palliative endoscopic procedures were performed in 72 of 172 (41.9 %) patients but only 14 (19,4 %) of the patients who required palliative drainage had a metallic stent implanted during their first endoscopic intervention, resulting in a high need for subsequent reinterventions) and a lack of pathological confirmation in 25,6% of the cases. Furthermore, only 12,7% of the patients received adjuvant chemotherapy and an additional 29% received palliative chemotherapy. The major limitation of our study was the high percentage of patients lost to follow up (62,2%), another surrogate marker for inadequate access to healthcare resources.

Conclusion: In conclusion, we identified several unmet needs in the current practices of oncological treatment for Romanian patients with biliopancreatic tumors. We believe significant efforts are required to improve the access to standard-of-care treatment for patient with BPT in low-resource medical systems, including audit efforts such as the one we carried out on in our study.

Disclosure: Nothing to disclose

P1026

CHARACTERISTICS AND OUTCOMES OF PATIENTS ADMITTED WITH ACUTE CHOLANGITIS: A TERTIARY HPB UNIT EXPERIENCE

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Introduction: Acute bacterial cholangitis is an infection of the biliary tree which is usually caused by an obstructed biliary system. Patient outcomes may be affected by availability of relevant expertise in the provision of biliary drainage. Tertiary hepatobiliary centres have the capability of providing definitive biliary drainage for patients with acute cholangitis.

Aims & Methods: We aim to assess the characteristics and outcomes of patients admitted with acute cholangitis to our tertiary centre in the United Kingdom. A retrospective analysis of patients admitted to our hospital

with acute cholangitis over a 3 year period from June 2016 to June 2019 was carried out. Patients were identified via our hospital's coding department by ICD-10 codes K83, K80.3 and K80.5. Individual case notes were analysed to exclude patients who did not meet Tokyo consensus criteria for diagnosis of acute cholangitis.

Results: The cohort consisted of 275 patients (53.3% female) with a median age of 72 years (range 19 - 97). The most common aetiology of cholangitis was choledocholithiasis (79%, n=218), followed by stent dysfunction (6.5%, n =18), malignant strictures without previous biliary intervention (5.8%, n=16) then benign strictures (4.3%, n=12) with the remaining patients having multiple aetiologies. 244 patients (88.4%) underwent a procedure to establish biliary drainage during their admission, of which 99.2% (n=242) was via ERCP. The median time from admission to ERCP was 4.9 days (range 0.3 - 35.5 days). Biliary cannulation and drainage was achieved in 94.2% of patients (n=228). The median length of stay was 8.2 days (range 1.4 - 123.6 days). Post-ERCP complications were observed in 5.4% of patients (n=13): post-sphincterotomy bleed (1.7%, n=4), pancreatitis (1.2%, n=3), cholangitis (0.8%, n=2), liver abscess (0.8%, n=2) and cholecystitis (0.4%, n=1) Neither in-hospital mortality nor 30-day all-cause mortality was observed in the patients who developed post-ERCP complications. The overall 30-day all-cause mortality rate was 4.7% (n=13) amongst our entire cohort of 275 patients and 2.8% (n=7) amongst the 242 patients who underwent ERCP.

Conclusion: Our data demonstrated that stone disease is the commonest cause of acute cholangitis in our cohort. ERCP is the commonest modality utilised to establish biliary drainage and has a high technical success rate with an acceptable complication rate.

Disclosure: Nothing to disclose

Poster presentations

Pancreas

Poster Presentations Pancreas

Pancreas

09:00-19:00 / Poster Exhibition

P1027

IN VITRO COMPARISON OF TWO ENCAPSULATED PANCREATIN PREPARATIONS

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Introduction: Kreon® (Mylan Healthcare) and Lipancrea® (Polfa Warszawa) are pancreatic enzyme supplements indicated in the treatment of exocrine pancreatic insufficiency.

Aims & Methods: In order to determine the interchangeability of both products, an in vitro comparison of their physical properties and enzymatic activity was carried out.

Amylase, Lipase and protease activities and lipase release at different pHs were assessed. In addition, capsule fill weight and particle size were determined.

Results: The length range of Kreon® and Lipancrea® pellets was 1-2 mm and 1.5-3.1 mm, respectively. Protease activity was below their label claim for Lipancrea® and above for Kreon® presentations. Further differences were observed in the kinetics of enzyme release. To prevent degradation of acid-sensitive enzymes in stomach, no enzymes should be released at pH < 5.5. While minimal or no release of lipase activity was observed at pH 1.0 and 4.0, a significant release was observed for Lipancrea® at pH 5.0, (41 % of actual lipase activity (aA) for Lipancrea® 8000; 21 % aA for Lipancrea® 16000) but not for Kreon®. Enzyme release at pH 5.0 can lead to enzyme degradation because of its limited stability at this pH range, and thus a reduction of the efficacy of the enzyme substitution. Enzyme release for Lipancrea® was generally slower than for Kreon® and seemed to be influenced by the preceding incubation at lower pH. Root cause for these differences in behaviour is most likely the qualitatively different enteric coating which is used to protect the enzymes from being released at low pH. It should also be noted that the two Lipancrea strengths show larger differences to each other than the two Kreon strengths tested.

Conclusion: Both products differ in their enzyme release characteristics. Therefore, their interexchange may result in therapeutic failure, as small differences in composition lead to significant differences in behaviour. In the absence of relevant clinical data, this in vitro dataset represents the most relevant evidence to judge on the interchangeability of both products. Based on this study, Kreon® seems to be more reliable than Lipancrea®, in terms of delivering the labelled enzyme amount to the patients.

Disclosure: All the authors are employees of Mylan Healthcare

P1028

SCREENING TOOLS FOR DIAGNOSING CYSTIC FIBROSIS-RELATED DIABETES - A NETWORK META-ANALYSIS

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Introduction: Improved life expectancy of cystic fibrosis (CF) patients has led to an increase in the prevalence of other complications, such as CF-related diabetes (CFRD). Currently used gold standard screening tool is the oral glucose tolerance test (OGTT) which is recommended to perform annually in all non-diabetic CF patients above the age 10.

Aims & Methods: We aimed to evaluate that these modalities may be potential alternatives for OGTT by performing a Bayesian diagnostic test accuracy network meta-analysis. We conducted a systematic search in five databases (MEDLINE, Embase, Web of Science, Scopus, CENTRAL). Eligible papers included study subjects previously diagnosed with CF and compared several diagnostic methods (as index tests), including Hemoglobin A1c (HbA1c) or continuous glucose monitoring (CGM) to OGTT (as reference standard). After data collection by two independent authors, we created 2x2 tables including true positive (TP), false positive (FP), true negative (TN) and false negative (FN) cells.

Results: Altogether, 31 papers reporting on 1236 patients were eligible for inclusion. The network consisted of 13 diagnostic modalities including CGM for different days (from 1 to 7), HbA1c, and etc. According to the ranking by superiority indices CGM for 2 days was ranked the highest. HbA1c, which is a commonly used, cheap, screening tool, was only ranked at the fifth place after CGM.

Conclusion: Based on our results, CGM might be a potential alternative for OGTT while we must be aware that it has its drawbacks (such as the cost and inconvenience of the device).

Disclosure: Nothing to disclose

P1029 WITHDRAWN

P1030

HNF6 IN HUMAN PANCREATIC DUCT DEVELOPMENT

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Introduction: The pancreas is both an exocrine and endocrine organ and plays a central role in digestion of food and regulation of blood glucose levels. Recently, we identified the novel diabetes gene *HNF6* regulating the transcriptional and epigenetic machinery critical for proper pancreatic endocrine development. In addition to a diabetic phenotype, patients lacking functional *HNF6* also suffered from pancreatic hypotrophy, in line with

exocrine pancreatic insufficiency, absence of gallbladder and of extrahepatic biliary duct. Moreover, HNF6 was shown to play an important role during duct morphogenesis in mice supporting a functional role during human pancreatic duct development. Therefore, we aim to investigate the underlying molecular basis by which loss of *HNF6* causes different pancreatic phenotypes in patients.

Aims & Methods: We used genome-edited human embryonic stem cells to dissect the functional consequences of defective *HNF6* in pancreatic ductal development. Specifically, we applied signaling molecules and growth factors inducing ductal cells, while inhibiting the respective counter lineage with inhibitors. This novel and unique approach yields virtually pure pancreatic duct-like cells resembling key features of adult human pancreatic ducts. Finally, various stages of development were characterized to assess the morphology, differentiation, and proliferation of HNF6-depleted ductal cells.

Results: During *in vitro* differentiation, loss of *HNF6* results in diminished formation of pancreatic progenitor (PP) cells. To efficiently initiate ductal differentiation, we purified PP cells using the stage-specific surface marker GP2. HNF6-depleted ductal organoids showed initially an increased cyst size similar to the mouse model but failed to maintain organoids in consecutive passages supported by loss of proliferation marker Ki67. Moreover, ductal organoids expressed markers such as CK19, CK8 and CFTR but showed increases in maturation marker CK7. This might correlate with an early decrease in NKX6.1 leading to premature formation of ducts and loss of proliferation capacity. Also, organoids lacking HNF6 tend to lose primary cilia during maturation in accordance with the mouse model.

Conclusion: Our *in vitro* approach to direct human HNF6-depleted PSCs towards pancreatic duct-like cells recapitulates aspects of patient phenotypes and therefore, provides a valuable methodology to characterize pancreatic diseases. However, further time-resolved RNA- and ATAC-seq analysis is necessary to reveal exact transcriptional and molecular mechanisms during ductal development.

Disclosure: Nothing to disclose

P1031

MODELLING JOHANSON-BLIZZARD SYNDROME IN A DISH

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Introduction: Johanson-Blizzard syndrome (JBS) is a rare genetic disorder with autosomal recessive inheritance. The condition is characterized by the association of congenital exocrine pancreatic insufficiency and aplasia of the nasal wings. We could previously identify mutations in the UBR1 gene encoding one of several E3 ubiquitin ligases of the N-end as the cause of disease. As mouse models incompletely recapitulate disease phenotype, novel models are warranted. Pluripotent stem cells present such an extraordinary powerful tool to investigate human embryonic development and to model human diseases.

Aims & Methods: We have generated two independent but complementary loss of function human embryonic stem cell lines by either deleting the entire UBR1 gene or the functional UBR1 box using CRISPR/CAS9 technology. In addition, induced pluripotent stem cells from two patients sharing a severe pancreas phenotype have been established and characterized.

Results: Stepwise pancreatic lineage differentiation of UBR1 mutant plu-

ripotent stem cells did not reveal obvious defects neither at the pancreatic progenitor nor at the undifferentiated state indicating an intact developmental program during early pancreatogenesis.

However, global quantitative proteomics revealed a stage-specific upregulation of a set of proteins in UBR1 ablated cells. Specifically, we could identify significant upregulation of certain proteins such as CHCHD2, MGMT, TXNRD2, and PNPO with described roles in cellular homeostasis. Whether these deregulated proteins are direct UBR1 substrates and are contributing to the JBS phenotype in the pancreas is part of our ongoing analysis.

Conclusion: In summary, the thorough analysis of our established JBS cellular models focusing on viability and cellular homeostasis together with quantitative proteome analysis will provide us a comprehensive picture of JBS in the pancreas.

Disclosure: Nothing to disclose

P1032

RECONSTRUCTION OF REGULATORY NETWORKS TO PREDICT GENE FUNCTION IN PANCREATIC DEVELOPMENT AND DISEASE

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Introduction: The complex dynamics establishing the three mature lineages (acinar, ductal, and endocrine) during pancreatic organogenesis are poorly understood and existing gene regulatory networks (GRNs) have been mostly obtained in rodent models from bulk-sequencing analytics. Albeit each compartment gives rise to a different set of diseases, there is a genetic overlap between pancreatic development and both pancreatic cancer as well as monogenic diabetes. Therefore, a better understanding of the cell-fate transitions that occur in the pancreas during normal development and disease could inform cell engineering efforts and lead to improved therapies. By reconstructing pancreatic GRNs, we aim to understand the perturbed programs in monogenic diabetes and boost cell engineering by the thorough understanding of the signals that guide differentiation in culture.

Aims & Methods: We applied Boolean network models which are widely used models for regulatory processes. In particular, when kinetic parameters of regulatory interactions in gene regulatory networks are not available. Initial modeling of the Boolean network regulatory functions was based on manual and text-mining approaches. We used tools such as BoolNet and ViSiBool to model, simulate, and visualize the Boolean networks. Next, we focused on real-valued time-series of RNA-seq data over the different pancreas developmental stages.

These data first required binarization, where we used the R-package BiTri-nA. Finally, the regulatory dependencies between components are inferred from the time-series data and integrated into the Boolean network.

Results: First, we developed an initial Boolean network model of *HNF6* signaling in pancreatic progenitor cells. This Boolean network model is based on extensive literature research and comprises 38 key genes which we identified in this research. Among these genes, we included regulators of pancreas development, such as *HNF6*, *NKX6.1*, *FOXA2*, *PDX1*, *SOX9*, and their regulators.

Then, we refined and extended the initial Boolean network using the previously described time-series omics data. Our extended network model was validated using knowledge from interaction databases and proved overall accurate. Finally, we apply this model to predict developmental changes during pancreas differentiation in cells depleted of known and novel diabetes genes. We plan to simulate loss of *HNF6*, a novel diabetes gene recently identified by our group and characterized using RNA- and

ATAC-seq, in order to predict transcriptional alterations for further validation. In the future, we will further expand this network with the input of bulk and single-cell-resolved transcriptional and chromatin dynamics data to elaborate the pancreatic lineages.

Conclusion: Our Boolean network reconstructing several stages of pancreas development is a valuable tool to predict gene function in the developing and diseased pancreas. This model provides the theoretical basis to understand the large-scale organization of the human pancreas - the principle to decode human pancreatic disease.

Disclosure: Nothing to disclose

P1033

CHLOROGENIC ACID REDUCES INFLAMMATION IN MURINE MODEL OF ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is characterized as a sudden inflammation with severe tissue injury in pancreas. The incidence of AP has been constantly rising and currently counts 20 to 80 per 100,000 per annum, with varying incidence rates reported from different countries, all increasing over the last 40 years. Although many researchers have attempted to identify the pathogenesis involved in the initiation and aggravation of AP, the disease is not still fully understood, and effective treatment is limited to supportive therapy. Many phytochemicals hold potential in improving AP symptoms and may be a valuable and effective addition to standard treatment of AP. Chlorogenic acid (CGA), a polyphenol found in coffee beans and different types of coffee, including green coffee, is known to have an anti-inflammatory effect. In this study, we investigated the effectiveness and therapeutic value of CGA for improving AP.

Aims & Methods: The primary aim was to examine the potential role of CGA in the treatment of experimental pancreatitis in mice. The AP murine model was induced by two intraperitoneal (i.p.) injections of L-arginine (dose 400mg/100g body weight (BW)), 1 hour apart. After 12h from the first L-arginine injection, mice were divided into 2 experimental groups: AP mice treated with CGA (oral gavage (p.o.) every 12h; 20 mg/kg BW), and non-treated AP mice (p.o. vehicle, i.e. 5% dimethyl sulfoxide (DMSO) every 12h). Control mice received equivalent volume of vehicle every 12h. Mice were kept under observation, allowed free access to chow and water, and sacrificed at 72h. Pancreatic and lung tissues were collected for histology in 4% buffered formalin or snap frozen in liquid nitrogen for myeloperoxidase (MPO) and amylase activity analysis.

Results: Administration of CGA (p.o., 20mg/kg BW) reduced MPO activity in pancreas and lungs as well as amylase activity in pancreas in murine mouse model of AP. Histological analysis revealed decreased severity of pancreatitis after CGA treatment compared to AP mice.

Conclusion: The results of the present study showed that CGA has an anti-inflammatory effect on L-arginine-induced pancreatitis. We suggest that dietary intervention with CGA could be recommended as supportive treatment in AP.

Disclosure: Nothing to disclose

P1034

SERUM IGG4 LEVELS OUTPERFORM IGG4/IGG RNA RATIO IN DIFFERENTIAL DIAGNOSIS OF IGG4-RELATED DISEASE

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Introduction: IgG4-related disease (IgG4-RD) is a chronic inflammatory-fibrosing disorder affecting virtually any organ, but most frequently the pancreaticobiliary system. Differential diagnosis is challenging due to a highly variable clinical presentation and relies on multiple diagnostic criteria rather than on single markers. Previously, qPCR-based measurements of the IgG4/IgG mRNA ratio that originate from dominant IgG4⁺ B-cell receptor (BCR) clones have been propagated as a critical endeavor to fill this diagnostic gap.

Aims & Methods: While promising, some shortcomings of this test were not addressed in the original work and further validation needed. We therefore performed IgG4/IgG qPCR on a cohort of IgG4-RD and non-IgG4-RD patients, validated results with a multiplex digital droplet PCR approach and compared test Performance to that of Serum IgG4 levels.

Results: In the current study, we demonstrated in concordance with de Vires et al. on independent cohorts and with different methodological setups that IgG4/IgG mRNA ratio is prone to false-positive results, which could cause misdiagnosis of pancreaticobiliary cancer. Furthermore, we found superior test accuracy of serum IgG4 levels, likewise not a perfect biomarker itself.

Conclusion: Therefore, our study questions the clinical benefit of IgG4/IgG mRNA ratios in the differential diagnosis of IgG4-RD in support of de Vires et al. but concurrently underpins the necessity for more reliable biomarkers to differentially diagnose IgG4-RD.

Disclosure: Nothing to disclose

P1035

THE ROLE OF THE TRANSCRIPTION FACTOR *TBX3* IN THE EMBRYONIC DEVELOPMENT OF THE MURINE PANCREAS AND REGENERATION OF ACUTE PANCREATITIS

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Introduction: Re-activation of genetic programs from early development is crucial for injury-induced organ regeneration. Interestingly, differentiation potential and self-renewal capabilities of pluripotent stem cells are shared features with tissue resident stem cells, a source of organ regeneration. *T-Box Transcription Factor 3* (*Tbx3*) has been shown to facilitate somatic reprogramming into induced pluripotent stem cells and act as a dynamic switch in activation of pluripotency, and thus stem cell renewal.

Aims & Methods: Therefore, we hypothesize that *Tbx3* is expressed and important during embryonic maturation of pancreatic development and favors regeneration of acute pancreatitis due to control of self-renewal capacity.

Results: Using a *Tbx3-Venus* reporter mouse strain, we showed that *Tbx3* expression is augmented at different stages during embryonic development of the pancreas and absent in adult pancreas. However, pancreas

specific deletion of *Tbx3* already at embryonic stage using a p48-Cre mouse line did not show any phenotypic differences of the architecture of the adult pancreas compared to their wildtype counterparts. Interestingly, induction of experimental acute pancreatitis by caerulein led to an upregulation of *Tbx3* expression during the regeneration phase.

Conclusion: Taken together, we observed *Tbx3* expression during embryonic development and again during acute pancreatitis. This may indicate that *Tbx3* favors tissue development and repair through regulation of stem cell compartments. To strengthen these initial findings, a detailed characterization throughout the regeneration of pancreatitis will shed light into the exact relevance of *Tbx3*.

Disclosure: Nothing to disclose

P1036

NEUTROPHIL TO LYMPHOCYTE RATIO TO PREDICT SEVERITY IN ACUTE PANCREATITIS: HOW DOES IT COMPARE WITH OTHER PROGNOSTIC SCORES

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Introduction: Acute pancreatitis' (AP) severity is based on the presence of organ failure and/or local or systemic complications. Although different scoring systems already exist, early prediction of severity is still a challenge. Neutrophil to lymphocyte ratio (NLR) is an early marker of inflammation that has been shown to correlate with acute pancreatitis' severity. **Aims & Methods:** Our aim was to investigate the association of NLR at admission with acute pancreatitis' severity, admission to the Intensive Care Unit (ICU), and death during hospitalization, as well as compare its accuracy as an early predictor of severity with other established prognostic markers/scores - haematocrit (HCT), blood urea, C-reactive protein (CRP), BISAP score and the modified Marshall Score (mMS).

A retrospective analysis of hospitalized patients with acute pancreatitis between 2018 and 2019 ($n=197$) was performed. Clinical outcomes included severity (according to the revised Atlanta Classification), admission to the ICU and death during hospitalization. For each of these outcomes, patients were divided in two groups and a t-test was performed to compare the NLR at admission in both groups. Age and aetiology were analysed as potential confounders through a logistic regression. A receiver operating characteristic (ROC) curve analysis was performed and the area under the curve (AUC) for NLR prediction of severity was compared with other established prognostic markers/scores' accuracy. A cut-off value of NLR for early prediction of severity was determined.

Results: Among the 197 patients admitted with acute pancreatitis, the leading aetiology was gallstones (81,22%, $n=160$) and only 30,46% ($n=60$) were considered moderate to severe. Twenty-seven patients (13,71%) were admitted to the ICU and six (3,05%) died during hospitalization. The NLR was significantly higher in the group of patients with moderate to severe pancreatitis (15,85 vs 8,11, $p<0.001$) as well as in the group of patients admitted to the ICU (15,66 vs 9,65, $p=0,02$). These differences remained significant after adjusting for age and aetiology (OR 1,09, 95%CI 1,04-1,13 for prediction of severity and OR 1,04, 95%CI 1,01-1,08 for ICU admission). No difference was found on the NLR of patients who died during hospitalization (16,13 vs 10,29, $p=0,4$).

The AUC for NLR prediction of severity was 0,72 (95%CI 0,64-0,80) and a cut-off value of $NLR>7,70$ was established (sensitivity 70,00% and specificity 64,23%). The AUC for the remaining markers was: BISAP score AUC 0,78

vs mMS AUC 0,77 vs Blood urea AUC 0,73 vs NLR AUC 0,72 vs CRP AUC 0,69 vs HCT AUC 0,59. Although the BISAP score seemed to be the most accurate predictor of severity in acute pancreatitis, its accuracy has not shown to be statistically significantly different from NLR ($p=0,19$).

Conclusion: A higher NLR was associated with moderate to severe acute pancreatitis and admission to the ICU. Although the BISAP score seems to be the most accurate predictor of severity, NLR uses the complete blood count alone and is not inferior to this compound score.

Disclosure: Nothing to disclose

P1037

PROGNOSTIC FACTORS OF SEVERE POST-ERCP PANCREATITIS - A MULTICENTER PROSPECTIVE COHORT STUDY

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Introduction: One of the most serious adverse events of endoscopic retrograde cholangiopancreatography (ERCP) is post-ERCP pancreatitis (PEP).

The incidence rate of PEP ranged from 3.5% to 9.7% in different clinical settings. There are numerous reports of prognostic factors for PEP, but no report has been published for prognostic factors associated with severe-to-fatal PEP.

Aims & Methods: The aim of this study is to investigate prognostic factors associated with severe-to-fatal PEP for biliary ERCP. The severity of PEP was defined by the lexicon for endoscopic adverse events [1]. The patients of biliary disease with intact papilla were prospectively enrolled at 36 centers from April 2017 through March 2018. Exclusion criteria were acute pancreatitis diagnosed before ERCP, altered gastrointestinal anatomy, and an ASA physical status greater than 3. The primary outcomes were the PEP incidence rates and its severity; mild, moderate, severe or fatal. The diagnosis and severity of PEP were defined by the lexicon for endoscopic adverse events. Univariate and multivariate logistic regression analyses were performed on patient-related factors, operator-related factors, procedure-related factors and preventive measures.

Results: A total of 15,732 ERCP procedures were performed in the 36 centers, and 3,739 ERCPs were enrolled in this study. The average of age was 72.5 years and 43.7% of patients were women. The overall success rate of bile-duct cannulation was 96.9%. The incidence rate of PEP was 6.9% (258 cases, which consist of 201 mild, 39 moderate, 17 severe and 1 fatal cases). Through the multivariate analyses, significant prognostic factors for severe-to-fatal PEP ($P < 0.05$) were the insertion of guidewire to the pancreatic duct (odds ratios (OR) 5.777 (95% CI, 1.105-30.206), $P = 0.038$), the administration of non-steroidal anti-inflammatory drug (NSAID) after the ERCP (OR 11.550 (95% CI, 3.720-35.857), $P < 0.001$), the past history of PEP (OR 7.558 (95% CI, 1.403-40.701), $P = 0.019$) and the scraping of bile duct (OR 5.758 (95% CI, 1.199-27.651), $P = 0.029$). The analysis showed that the significant preventive measures of severe-to-fatal PEP were the endoscopic sphincterotomy (EST) (OR 0.177 (95% CI, 0.060-0.523), $P = 0.002$) and the endoscopic pancreatic stenting (EPS) (OR 0.094 (95% CI, 0.011-0.770) $P = 0.028$).

The analysis showed that the significant prognostic factors of severe-to-fatal PEP compared to mild-to-moderate PEP were the biliary cannulation with the guidewire placement to the pancreatic duct (OR 4.008 (95% CI, 1.263-12.714), $P = 0.019$) and the administration of NSAID after the ERCP (OR 6.102 (95% CI, 1.619-23.008), $P = 0.008$). The EST was shown to be significant preventive measures of severe-to-fatal PEP compared to mild-to-moderate PEP (OR 0.288 (95% CI, 0.092-0.897), $P = 0.032$).

Conclusion: In the biliary ERCP, the insertion of guidewire to the pancreatic duct and the administration of NSAID after the ERCP were the risk for severe-to-fatal PEP, whereas the EST and the EPS were supposed to be preventive measures of severe-to-fatal PEP.

References: [1] Cotton PB, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc* 2010; 71: 446-454.

Disclosure: Nothing to disclose

P1038 WITHDRAWN

P1039

RISK PREDICTION MODEL FOR DEVELOPING PANCREATIC NECROSIS

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Introduction: Necrosis is a major local complication in acute pancreatitis which affects its outcome.

Aims & Methods: Our aim was to evaluate the clinical characteristics of acute necrotizing pancreatitis (ANP) and to design a predictive model for that. The Hungarian Pancreatic Study group has prospectively collected multicenter clinical data of 1435 adult patients between 2012 and 2017. 1429 of them contained valuable data on pancreatic necrosis and were enrolled. Statistical analyses compared pancreatitis with (ANP) and without necrosis (AP). Predictive models were built by the Random Forest approach.

Results: 9.31% (n=133) of the patients had ANP. As expected ANP was associated with higher mortality (8.27% vs 1.93%; $p < 0.0001$), more severe disease (mild: 0.00% vs 75.69%, moderate: 73.68% vs 20.91%, severe: 26.32% vs 3.40%), longer hospitalization (22.95±19.23 days vs 10.18±7.22 days; $p < 0.0001$), and higher rate of complications (pseudocyst: 30.83% vs 6.34%, $p < 0.0001$; diabetes: 13.53% vs 3.24%, $p < 0.0001$; respiratory failure: 20.45% vs 3.27%, $p < 0.0001$; heart failure: 8.33% vs 1.17%, $p < 0.0001$; renal failure: 15.19% vs 1.71%, $p < 0.0001$). Several risk factors were identified among admission parameters. After combining these parameters, we created a predictive model with the Random Forest approach that does not include false negative cases.

Conclusion: Pancreatic necrosis markedly influences the outcome of acute pancreatitis. Without the presence of false negative cases, our model is able to rule out development of ANP in this derivation cohort. After the validation of our result, we will translate it into a predictive bioinformatics tool to help physicians in assessing risk of this severe complication.

Disclosure: Nothing to disclose

P1040 WITHDRAWN

P1041

PREDICTIVE SCORE DEVELOPMENT FOR A CLINICAL TRIAL ON THE PRE-EMPTIVE USE OF EXTRACORPOREAL CYTOKINE REMOVAL WITH CYTOSORB THERAPY IN ACUTE NECROTIZING PANCREATITIS

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Introduction: In severe acute pancreatitis (SAP) dysregulated hyperinflammation can rapidly progress into multiple organ failure (MOF) with high mortality. CytoSorb is a promising treatment to attenuate hyperinflammation and improve outcomes.

Aims & Methods: To design a prospective randomized controlled trial to assess the effects of early CytoSorb treatment on the prevention of disease progression. In the first phase, we developed a predictive score to identify SAP patients at risk of developing MOF.

Methods: For risk assessment, the recently developed Cytoscore by Kogelman et al. 2019. was modified. The Procytoscore (PCS) includes oxygen requirement, lactate levels, procalcitonin levels, and vasopressor dosage and changes within 6 hours. For the development we used the retrospective data of 40 SAP patients admitted to the intensive care unit (ICU) of Medical School, University of Pécs from 2018-2019.

Results: Patients were 66 ± 16 years old, 57.5 % required mechanical ventilation, 70% needed vasopressor support. Mortality was 55 % and length of ICU stay was 10 (range: 1-72) days. PCS in the whole cohort was; median: 4.5 range: 0-14. Using Mann-Whitney U test, non survivors had higher PCS than survivors: median (range): 7 (1-14) vs. 3 (0-8) (p=0,0002). The PCS for other outcomes did not differ significantly.

Conclusion: PCS significantly differentiated survivors from non survivors, therefore it may have potential to be used as a new, easy tool for patient selection for the planned trial. The next step is the validation of PCS on a larger dataset to determine the best cut-off values to predict progression to MOF.

References: Kogelmann et al. Evaluating a Cytosorb Score in septic shock (ECSISS) 2019 Infection

Disclosure: Nothing to disclose

P1042

INSUFFICIENT DECISION MAKING PROCESS CONCERNING THE START OF ENTERAL FEEDING IN ACUTE PANCREATITIS

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Introduction: In order to reduce mortality in acute pancreatitis (AP), enteral feeding (EF) is recommended in the severe or predicted severe form of the disease. We aimed to investigate the factors leading to the decision to start enteral feeding and the associations between enteral feeding and the outcome of the disease.

Aims & Methods: 1421 prospectively collected cases from 12 countries were included in the analysis. EF and Non-EF patient groups were formed accordingly. We have investigated the associations between the pancreas and inflammation related laboratory parameters (amylase, lipase, C-reactive protein-CRP, white blood cell count-WBC, lactate dehydrogenase-LDH), imaging findings of the pancreas (necrosis, fluid collection, pseudocyst) and symptoms (abdominal pain, vomiting, fever) in relation to the start of EF.

Results: Enteral feeding was applied during hospitalization in 26% of mild, 64% of moderately severe and 77% of severe cases. High level of CRP (EF:61,6mg/L(Q1-Q3:16-167,1); Non-EF:43,6mg/L(Q1-Q3:9,8-123,3); p=0,039), WBC (EF:12,3G/L(Q1-Q3:10,2-16,3); Non-EF:11,3G/L(Q1-Q3:8,3-14,6); p=0,003), LDH (EF:397U/L(Q1-Q3:306,8-524); Non-EF:351,8U/L(Q1-Q3:240,3-478,3); p=0,046), the presence of necrosis, pseudocyst, fluid collection (all with p< 0,001) and the intensity of abdominal pain (p<0,01) were associated with the start of EF. Unfortunately, enteral feeding was not applied in 23% of the severe cases and the mortality was almost double in this group compared to the EF group (53% vs. 28%).

Conclusion: Decision mechanisms of starting EF seems logical, however, there remains substantial proportion of patients with severe AP without EF. Since EF is cost effective and has very low complication rate if applied correctly, it can be recommended in all cases of AP regardless of laboratory parameters and imaging findings.

Disclosure: Nothing to disclose

P1043

DISRUPTION OR DISCONNECTION OF THE PANCREATIC DUCT IN PATIENTS WITH SEVERE ACUTE PANCREATITIS: A LARGE PROSPECTIVE MULTI-CENTER COHORT

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Introduction: Disruption or disconnection of the pancreatic duct is a common finding following severe pancreatitis. Studies on this topic represent small and selected subgroups of patients undergoing specific interventions with limited data from observational studies on the exact incidence, clinical impact, optimal diagnostic work-up and treatment strategies. Therefore, we investigated disruption or disconnection of the pancreatic duct in a large unselected cohort of patients with severe acute pancreatitis.

Aims & Methods: A total of 927 consecutive patients with severe acute pancreatitis as defined by the revised Atlanta Classification, who were included in a prospective database from November 2005 until December 2015 in 25 centers of the Dutch Pancreatitis Study Group, were evaluated for disruption or disconnection of the pancreatic duct. We assessed patient characteristics, characteristics of pancreatic fistula, diagnostic modalities, invasive interventions and clinical impact of disruption or disconnection of the pancreatic duct. Generalized linear models were used to adjust for pre-specified confounders (i.e. age, sex, (infected) necrosis and organ failure).

Results: Disruption or disconnection of the pancreatic duct was diagnosed in 261/927 patients (28%). Overall mortality in these patients was 12%. Characteristics of disruption or disconnection and the different diagnostic modalities and invasive interventions used are summarized in Table 1. Male gender (OR 1.5, 95% CI 1.1 - 2.1, p=0.008) and parenchymal

necrosis (OR 4.6, 95% CI 3.2 - 6.7, p<0.001) were associated with disruption or disconnection of the pancreatic duct. Multivariate logistic regression models were fit to ascertain the independent effect of a disrupted or disconnected pancreatic duct on mortality beyond the first week (adjusted OR 0.7, 95% CI 0.4 - 1.1, p = 0.143), readmission (adjusted OR 1.8, 95% CI 1.2 - 2.7, p=0.003), infected necrosis (adjusted OR 9.7, 95% CI 6.1 - 15.4, p<0.001), need for invasive intervention (adjusted OR 10.6, 95% CI 5.5 - 20.5, p<0.001) and organ failure (adjusted OR 1.7, 95% CI 1.2 - 2.4, p=0.003). There was also an independent association with abdominal compartment syndrome (adjusted OR 3.1, 95% CI 1.3 - 7.4, p=0.009), and endocrine and exocrine pancreatic insufficiency (adjusted OR 1.5, 95% CI 1.0 - 2.1, p=0.043 and adjusted OR 1.5, 95% CI 1.0 - 2.2, p=0.041).

Conclusion: Around one third of patients with severe acute pancreatitis develop disruption or disconnection of the pancreatic duct. Male gender and pancreatic parenchymal necrosis appear to be predisposing factors. Diagnostic modalities and treatment strategies vary widely in daily practice and the clinical impact is considerable. Efforts should be made to define an optimal diagnostic work-up and treatment strategy to improve outcomes.

Disclosure: Nothing to disclose

P1044

PANCREATIC INVOLVEMENT IN VIRAL HEPATITIS INFECTION: SYSTEMATIC REVIEW OF PRESENTATION, DIAGNOSIS AND TREATMENT

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Introduction: Although viral hepatitis (HAV, HBV, HCV, HEV) are well-researched and often met in everyday clinical practice, pancreatic involvement in such patients is a relatively rare clinical entity. We conducted a systematic review in order to summarize currently available data on pancreatic involvement in patients affected by viral hepatitis.

Aims & Methods: A comprehensive literature search of Medline, Scopus and ISI Web of Science databases was conducted in order to identify papers reporting cases of pancreatic involvement in patients affected by viral hepatitis. The eligibility criteria for inclusion in the review required that study reports of patient(s) affected by viral hepatitis with pancreatic involvement, and that individual data on age, gender, clinical presentation and outcome are available.

Results: In total, 45 studies reporting data on 72 patients were included in the analysis. The majority of patients were males (69.0%) diagnosed at a mean age of 24.99±16.06. Most of the cases were diagnosed in Asia (56.9%, in India 52.8%), followed by North America (23.6%), Europe (13.9%), South America (4.2%) and Africa (1.4%). Most of the patients were affected by HAV (41.6%), followed by HEV (29.2%), HBV (8.3%), and HCV (1.4%), while 19.4% at the time of diagnosis were classified as affected by "hepatitis virus". Among potential risk factors, most frequently present was immunosuppression (4.2%) while alcohol and/or i.v. drugs intake and chronic diseases were present in only a small portion. Pancreatic involvement exclusively presented itself in the form of acute pancreatitis (100.0%), that in 66.7% was mild while in 33.3% was severe. Necrotizing pancreatitis developed in 6 (8.3%) patients, pseudocyst in 4 (5.6%), while in 1 patient (1.4%), diagnosis of chronic pancreatitis was set during the follow-up. Apart from liver and pancreas, respiratory system was affected in 2.8% of patients, 6.9% encountered a renal failure, while 5.6% experienced a multiorgan

dysfunction syndrome (MODS). Elevated lipase and amylase, when reported, were present in 100% and 98.3% of patients respectively (when reported). All the patients had features characteristic for pancreatitis on abdominal imaging examination. Apart from being treated conservatively, 4 patients (5.6%) needed surgery. Despite the treatment 22.5% of patients died.

Conclusion: Increased awareness of pancreatic involvement in viral hepatitis is needed, especially because it can have substantially impact on therapeutic approach and outcome in patients affected.

Disclosure: Nothing to disclose

P1045 WITHDRAWN

P1046

CORRELATION OF INFLAMMATORY MARKERS WITH RAISED INTRA ABDOMINAL PRESSURE IN PATIENTS WITH ACUTE PANCREATITIS: A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Intra abdominal hypertension (IAH) is a significant factor influencing outcome in patients with severe acute pancreatitis (AP) and is considered a sequelae of inflammatory cascade. Few studies exists studying the interplay between inflammatory markers and intra-abdominal pressure (IAP) and hence we planned to study the same.

Aims & Methods: In a prospective observational study, 118 patients of AP presenting within first week of illness were included. IAP and inflammatory markers including C-reactive protein (CRP), procalcitonin, interleukin-6 (IL-6) & interleukin-10 (IL-10) were measured at day 1, 3 & 7 of admission, day of percutaneous drain (PCD) and after 48 hours of PCD. IAH was defined as IAP persistently >12 mmHg and abdominal compartment syndrome (ACS) was defined as IAP persistently >20 mmHg with new or worsening organ failure. Inflammatory markers were compared between IAH versus non IAH and ACS versus non ACS groups. ROC curves were analysed for prediction of IAH at different time interval. Patients were managed using a step up approach with PCD being the first step of intervention. Baseline characteristics, severity measures and outcome measures were analysed.

Results: Out of 118 patients, 46 (39%) patients had IAH and 10 (8.5%) patients had ACS. Baseline characteristic were comparable between except obesity and diabetes were more common in IAH group. Presence of IAH was associated with poor prognosis in form of prolonged hospital stay, ICU stay and need of PCD (p < 0.05 for all). Also fall of IAP was associated with better outcome. Levels of inflammatory markers were higher in IAH group at defined time intervals (Table).

After PCD insertion mean IAP levels decreased from 14.5 to 12.6 mmHg (p < 0.001) along with reduction of procalcitonin (p = 0.09), CRP (p = 0.02) and IL-6 (p = 0.05). Patients with ACS had persistently elevated inflammatory markers even after PCD. Median values of procalcitonin (0.38 versus 3.67 ng/ml, p = 0.02), CRP (89 versus 156 mg/L, p = 0.004), and IL-6 (66.5 versus 310 pg/ml, p = 0.03) were higher in ACS group at 48 hours after PCD. On ROC analysis, best predictors of IAH were IL-6/IL-10 ratio (AUC 0.7, 68% sensitivity & specificity) at admission, CRP (AUC 0.75, 78% sensi-

tivity & 70% specificity) at 48 hours, IL-6 (AUC 0.74, 57% sensitivity & 80% specificity) at day 7 and IL-6 (AUC 0.8, 64% sensitivity & 80% specificity) post PCD.

Conclusion: Inflammatory markers were significantly elevated in patients of IAH and reduction of IAP after PCD insertion was associated with reduction of inflammatory markers. Significantly inflammatory markers remained persistently elevated even after PCD in case of ACS.

Inflammatory marker Median (IQR)	Normal IAP group	Raised IAP group	p value
Procalcitonin (ng/ml) At admission (n=117)	0.312 (0.132-0.694)	0.976 (0.36-1.56)	<0.001
Procalcitonin (ng/ml) At 48 hours (n=113)	0.138 (0.038-0.42)	0.9 (0.37-3.48)	<0.001
Procalcitonin (ng/ml) At Day 7 (n=48)	0.130 (0.033-0.28)	0.637(0.227-2.34)	<0.001
Procalcitonin (ng/ml) Post PCD (n=50)	0.200 (0.085-8.92)	1.10 (0.208-7.87)	0.06
CRP (mg/L) At admission (n=116)	167.5 (60.5-233.6)	212.3 (144.2-300.2)	0.003
CRP (mg/L) At 48 hours (n=112)	113.8 (30.7-137.2)	188 (147.9-310)	<0.001
CRP (mg/L) At Day 7 (n=48)	65 (37.9-118.2)	161 (112-272)	<0.001
CRP (mg/L) Post PCD Day 3 (n=50)	76.30 (51.5-181.2)	151.00 (63.2-255)	0.391
IL- 6 (pg/ml) At admission (n=118)	57.5 (14-189)	190 (72-441)	<0.001
IL- 6 (pg/ml) At 48 hours (n=105)	36 (13-72)	144 (53-295)	<0.001
IL- 6 (pg/ml) At Day 7 (n=42)	30 (8-56.5)	55 (33-189)	0.005
IL- 6 (pg/ml) Post PCD Day 3 (n=48)	58.00 (10.5-170)	72.00 (33.5-254)	0.379
IL-6/IL-10 At admission (n=47)	7.7619 (3.35-21.01)	20.00 (6.10-45.41)	0.034
IL-6/IL-10 At 48 hours (n=30)	5.5 (2.9-17.3)	13.5 (4-31.11)	0.171
IL-6/IL-10 At day 7 (n=13)	5.0 (7.8-10)	10.3 (3.8-16)	0.056
IL-6/IL-10 Post PCD Day 3 (n=26)	4.6 (1.31-7.37)	9.33 (2-17.35)	0.319

[Table. Levels of inflammatory markers in normal IAP versus IAH Groups]

Disclosure: All the authors have no potential conflicts of interest to disclose with respect to research, authorship and presentation of this article

P1047

NON-ALCOHOLIC FATTY LIVER DISEASE WORSENS THE OUTCOME IN ACUTE PANCREATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: The prevalence of fatty liver disease (FLD) and that of non-alcoholic fatty liver disease (NAFLD) share some risk factors known to exacerbate the course of acute pancreatitis (AP).

Aims & Methods: This meta-analysis aimed to investigate whether FLD or NAFLD carry a higher risk of untoward outcomes in AP.

This study was registered on PROSPERO under registration number CRD42019123416. We conducted our meta-analysis in accordance with PRISMA guidelines. We performed a systematic search in seven medical databases for cohort studies that compared the outcomes of AP for the presence of FLD or NAFLD and reported inhospital mortality, AP severity, length of hospital stay and/or local complications.

We calculated pooled odds ratio (OR) or weighted mean difference (WMD) with 95% confidence interval (CI) for FLD vs. no-FLD and NAFLD vs. no-NAFLD comparisons.

Results: We included 13 articles in our meta-analysis. AP patients with FLD were more likely to die (5.09% vs 1.89%, OR=3.56, CI=1.75-7.22), develop severe AP (16.33% vs 7.87%, OR=2.67, CI=2.01-3.56), necrotizing pancreatitis (34.83% vs 15.75%, OR=3.08, CI=2.44-3.90) and had longer in-hospital stay (10.8 vs 9.2 days, WMD=1.46, OR=0.54-2.39). The odds of the composite of moderately severe and severe AP (OR=2.64, CI: 1.37-5.11) and severe AP alone was higher in the NAFLD group (OR=2.21, CI: 1.70-2.88). Patients with NAFLD tended to have longer hospital stay (WMD=1.41 days, CI: 0.03-2.79 days). Both FLD and NAFLD proved to be independent risk factors of a more severe disease course (OR=3.68, CI=2.16-6.29 and OR=3.39, CI=1.52-7.56 for moderate/ severe vs. mild AP, respectively).

Conclusion: FLD and NAFLD worsen the outcomes of AP, which suggests that incorporating FLD or NAFLD into prognostic scoring systems of AP outcomes might improve the prediction of severity and contribute to a more individualized patient care.

Disclosure: Nothing to disclose

P1048 WITHDRAWN

P1049 WITHDRAWN

P1050 WITHDRAWN

P1051

EARLY RESULTS OF A PROSPECTIVE COHORT ANALYSIS- ASSOCIATION OF LOW ALBUMIN LEVELS AND MORTALITY IN ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is still associated with significant morbidity and mortality worldwide. Thus, the early identification of high-risk patients is critical. Hypoalbuminemia was shown to be independently associated with persistent organ failure and death in retrospective AP cohorts.

Aims & Methods: Our aim was to validate the correlation between on-admission serum albumin levels and clinical outcomes of AP in a large prospective multicenter cohort. The Hungarian Pancreatic Study Group (HPSG) has prospectively enrolled patients with diagnosis of AP from 12 countries and 26 centers from 2012 to 2018. Patients were divided into low and normal albumin groups, the cutoff being 35 g/L. We used Chi-square test, Mann-Whitney-U test and receiver operating characteristic curve analysis.

Results: From the validated cases, 822 patients had on-admission albumin levels. With 58% males, mean age of 55.7 years, 20% severe and 6% moderately severe cases, 2.6% mortality rate this cohort proved to be representative of the general characteristics of the disease. Older age, alcoholic etiology and more comorbidities were characteristic of the low albumin group. Mortality was significantly higher in this group (4.7% and 1.9%, p=0.045). Also, a tendency of more severe and moderately severe cases was seen in the low albumin group (p=0.056). From on-admission laboratory parameters, patients had significantly lower eGFR and calcium and higher CRP values (p< 0.001 in all cases). ROC analysis for mortality resulted in an AUC of 0.71 (95% CI: 0.619-0.801).

Conclusion: The overall predictive value of albumin for mortality in our cohort was acceptable, but not as strong as previously reported.

Disclosure: Nothing to disclose

P1052 WITHDRAWN

P1053

RECURRENT ACUTE PANCREATITIS PREVENTION BY THE ELIMINATION OF ALCOHOL AND CIGARETTE SMOKING (REAPPEAR): PROTOCOL OF A RANDOMIZED CONTROLLED TRIAL AND A COHORT STUDY

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Introduction: Alcohol-induced acute recurrent pancreatitis (ARP) is a preventable and potentially chronic condition, which significantly lowers quality of life. Both alcohol and tobacco abuse are independent risk factors for ARP and chronic pancreatitis. Due to the lack of evidence, current guidelines on the management of pancreatitis fail to give detailed recommendations on prevention.

Aims & Methods: The REAPPEAR Study consists of an international multicenter randomized controlled trial (REAPPEAR-T) and a prospective cohort (the REAPPEAR-C), with a 2 year follow-up, recruiting patients hospitalized for alcohol-induced acute pancreatitis (AP). The same eligibility criteria and outcomes will be used in both cases, the primary end-point of the study being the recurrence of AP. At every pre-scheduled visit, participants' addiction and motivation to change will be evaluated with questionnaires.

Furthermore, laboratory testing, physical assessment and biologic sample collection will be conducted. Socioeconomic status and quality of life will also be evaluated at given time points.

All patients will receive a standard intervention delivered by a nurse before enrollment as part of standard therapy, on the topics of alcohol and smoking cessation. In the trial, patients will be randomized either to the repeated intervention group or the non-repeated intervention group and attend visits at 3, 6, 12, and 18 months. The repeated intervention group will receive a similar intervention at every visit according to the study schedule.

Patients of the REAPPEAR-C will attend only a 12-month visit and one at study close-out at 24 months. They will not receive repeated interventions. In the cohort, the combined and separate effects of alcohol and smoking cessation will be evaluated on recurrence.

Results: The primary endpoint of the REAPPEAR Study will be the recurrence of AP irrespective of etiology (given as rate of event) and/or mortality within 2 years. Secondary endpoints include overall and alcoholic recurrence (rate and cumulative incidence), length of hospital stay, reduction of smoking and alcohol consumption (biomarker levels and self-reported consumption), changes of blood pressure and BMI. The cost-effectiveness of the intervention program will be evaluated based on health-care costs.

Conclusion: The REAPPEAR study examines preventive measures in alcohol-induced recurrent acute pancreatitis. The REAPPEAR-T investigates how a combined, repeated intervention program influences recurrence and the REAPPEAR-C will provide details on how much alcohol and smoking cessation separately and combined lower the risk of a new episode of AP.

Disclosure: Nothing to disclose

P1054

WHAT ARE THE OUTCOMES OF LIVER TRANSPLANT PATIENTS WHEN HOSPITALIZED WITH ACUTE PANCREATITIS?

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Introduction: Acute pancreatitis (AP) has been recognized as a serious complication in liver transplant (LT) recipients with previous reports of increased morbidity, mortality and in severe cases, even graft rejection. We sought to investigate in-hospital outcomes of patients with previous LT that are admitted for AP.

Aims & Methods: The 2016 and 2017 National Inpatient Sample (NIS) database was queried for all discharges using ICD10-CM/PCS codes of AP of any etiology and those with a secondary diagnosis of prior liver transplant (LT). Patients were divided amongst those with LT and non-LT. Primary outcome was in-hospital mortality. Secondary outcomes were hospital length of stay (LOS), acute kidney injury (AKI), mechanical ventilation, systemic inflammatory response (SIRS), hospital related charges and costs. Multivariate regression analysis model was used to adjust for potential confounders

Results: 575,230 admissions with AP were identified which 0.2% (n=629) had prior LT. Patients with LT were more likely to have a Charlson comorbidity index of ≥ 3 (55.6% vs 15.5%; $P < 0.01$), to have Medicare as primary payer (56.4% vs 30.8%; $P < 0.01$), to be admitted to a large referral hospitals (67.5% vs 45.9%; $P < 0.01$), in urban areas (93.7% vs 87.8%; $P < 0.01$) and to teaching hospitals (76.2% vs 59.9%; $P < 0.01$). Patient with LT were less likely to have concomitant alcohol abuse disorder (13.5% vs 29.8%; $P < 0.01$). LT patients hospitalized with AP did not have higher mortality (aOR 1.00), but did have a shorter LOS [-1.71 day; ($P < 0.01$)], and higher rates of AKI [aOR 1.67; ($P = 0.02$)]. No significant difference was found in total hospitalization charges, cost or in any of the other secondary outcomes.

Conclusion: Liver transplant patients may not be associated with higher AP-related mortality or worse clinical outcomes when compared to those without a history of LT. However, LT was found to be associated with AKI. LT patients in the US have good outcomes when hospitalized with AP but the etiology of higher rates of AKI remains unclear and needs to be investigated.

Disclosure: Nothing to disclose

P1055

PRIORITIZATION OF CHOLECYSTECTOMY AFTER ACUTE BILIARY PANCREATITIS: IS RECURRENCE PREDICTABLE?

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Introduction: The gold standard approach to acute biliary pancreatitis (ABP) includes the recommendation for cholecystectomy during the index admission, which is not always followed, due to the large number of patients. Previous research has linked some clinical and analytical variables with the risk of recurrence of ABP. Our aim was to identify risk factors for recurrent ABP to help prioritize patients for cholecystectomy.

Aims & Methods: Retrospective single center study, including patients admitted due to a first episode of ABP from 01/01/2017 to 31/10/2019. Patients with previous cholecystectomy were excluded, as well as those submitted to cholecystectomy in the index admission. Biliary aetiology was defined by the presence of lithiasis/microlithiasis in the common bile duct/gallbladder in imaging studies and/or occurrence of an acute rise in alanine aminotransferase (> 150UI/L) without other probable cause. The primary outcome was the 6-month recurrence rate after the index ABP.

Results: 241 patients were included, with a mean age of 69,3 (±17,3) years and female predominance (58,1%). Median time for cholecystectomy was 153 days. Recurrent biliary pancreatitis occurred in 46 patients (19,1%), with a median time to recurrence of 81 days. Patients with more comorbid conditions (namely with Charlson comorbidity index ≥ 4) presented higher risk of severe/moderately severe recurrent pancreatitis (p=0,045). Demographic and analytical factors, as well as index ABP severity, were not associated with the overall risk of recurrence. Endoscopic retrograde cholangiopancreatography with sphincterotomy did not prevent recurrent ABP. Recurrence of biliary complications occurred in 5,4% of patients (cholangitis: 2,9%; cholecystitis: 2,1%; obstructive jaundice: 1,7%) and was associated with organ failure at the index ABP (p=0,006).

Conclusion: ABP has a considerable recurrence risk in patients waiting for cholecystectomy. Overall recurrence was not associated with any of the demographic or analytical tested variables. Patients with more comorbidities presented a higher risk of severe recurrence. On the other hand, patients with organ failure at the index ABP had an increased incidence of recurrent biliary complications. These patients may be considered as priority groups for earlier cholecystectomy.

Disclosure: Nothing to disclose

P1056

NICOTINE PROMOTES ACTIVATION OF PANCREATIC STELLATE CELLS THROUGH INDUCING AUTOPHAGY

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Introduction: Nicotine is widely considered as an independent risk factor of pancreatic fibrosis, but the mechanism is still unclear. Pancreatic stellate cells (PSCs) are the main functional cells leading to pancreatic fibrosis. Recent researches have shown that activation of PSCs can change along with the alteration of autophagy. Our study was aimed to explore the effects of nicotine on pancreatic stellate cells (PSCs).

Aims & Methods: Primary human PSCs and rat PSCs were cultured and treated with nicotine (0.1 μM and 1 μM). The proliferation, apoptosis, α-SMA expression, extracellular matrix metabolism and autophagy of PSCs were detected by CCK-8 assay, flow cytometry, real-time PCR and Western blotting analysis.

Results: The proliferation, α-SMA expression and autophagy of hPSCs and rPSCs were significantly promoted by nicotine. Meanwhile, the apoptosis of hPSCs and rPSCs was significantly reduced. The extracellular matrix metabolism of hPSCs and rPSCs was also regulated by nicotine.

Conclusion: Our finding suggests that nicotine can promote activation of pancreatic stellate cells (PSCs) through inducing autophagy, providing a new insight into the mechanisms by which nicotine affects pancreatic fibrosis.

Disclosure: Nothing to disclose

P1057

EUS-GUIDED BIOPSY OF HEALTHY PIG PANCREAS: A PROSPECTIVE, SINGLE-BLIND COMPARATIVE STUDY OF DIFFERENT NEEDLES. TOWARDS THE HISTOLOGICAL DIAGNOSIS OF EARLY CHRONIC PANCREATITIS

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Introduction: Diagnosis of early chronic pancreatitis (CP) is a challenge due to the lack of accurate diagnostic methods. EUS-guided biopsy is used for the histological diagnosis of solid pancreatic lesions, and it is able to diagnose advanced CP. However, the ability of EUS-guided biopsy to obtain pancreatic core tissue in patients with minimal changes of CP and its potential use for the histological diagnosis of early CP is unknown.

Aims & Methods: Aim of the study was to evaluate the ability of different EUS-guided biopsy needles to obtain histological samples of healthy pig pancreas. Methods: A prospective, single-blind comparative study was performed in two pigs, 2 months old, and 22 Kg weight. EUS was performed under general anesthesia with a therapeutic echoendoscope (PENTAX-3870UTK) and a HITACHI ultrasound system. A biopsy was taken from the body of the pancreas with commercially available needles (SharkCore™ Medtronic; Acquire™ Boston Scientific; SonoTip TopGain® Mediglobe; ProCore™ Cook-Medical) of all available sizes. Two passes with 10 to-and-fro movements each were done with each needle. Samples were collected in Cytolite® solution, coded and blindly evaluated by expert pathologists. The presence of tissue core, fragmentation, core size, amount of blood and sample quality for histological assessment were analyzed.

Results: Results are shown in table

Conclusion: Obtaining a core tissue of healthy pancreas by EUS-guided biopsy is feasible with the ProCore™ 20-gauge, Acquire™ and SharkCore™ 19-gauge and 22-gauge, and SonoTip TopGain® 19-gauge needles. Whether EUS-guided biopsy with these needles is accurate and safe for the histological diagnosis of early CP deserves further investigations.

Type of needle and caliber	Core	Fragmentation	Size (cm)	Blood	Quality
SharkCoreTM 22-gauge	Yes	High	0.2	++	Satisfactory
SharkCoreTM 25-gauge	No	High	0.1	++	Unsatisfactory
SharkCoreTM 19-gauge	Yes	High	0.3	+++	Satisfactory
AcquireTM 22-gauge	Yes Yes	High	0.2	++	Satisfactory
AcquireTM 25-gauge			No tissue		
AcquireTM 19-gauge	Yes	High	0.4	+++	Satisfactory
SonoTip TopGain® 22-gauge	Yes	High	0.1	+++	Unsatisfactory
SonoTip TopGain® 25-gauge			No tissue		
SonoTip TopGain® 19-gauge	Yes	High	0.3	+	Satisfactory
ProCoreTM 20-gauge	Yes	Medium	0.3	-	Satisfactory

[Table 1]

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P1058

EVIDENCE FOR DIAGNOSIS OF EARLY CHRONIC PANCREATITIS AFTER THREE EPISODES OF ACUTE PANCREATITIS

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Introduction: Chronic pancreatitis (CP) is an end-stage disease with no specific therapy; therefore, an earlier diagnosis has crucial importance.

Aims & Methods: We hypothesized that recurrent acute pancreatitis (RAP) is an intermediate stage between acute pancreatitis (AP) and CP. Prospectively collected international clinical dataset of 1,349 patients and an experimental pancreatitis model were used. 102 clinical and laboratory biomarkers were compared across AP (non-CP), RAP (non-CP), and CP groups. Concerning the experimental part of the study, repetitive injections of cerulein were applied to mimic the CP development via recurrent attacks.

Results: In the AP registry, 983 patients had a single attack of AP (non-CP), 304 had earlier attacks (RAP2-14, non-CP), whereas 62 had earlier developed CP. 0% of CP was diagnosed among patients with a single AP episode, 1% with RAP2, 16% with RAP3, and 50% with RAP4+. Fifteen of the investigated factors (epidemiology, etiology, laboratory- and pancreas-based parameters) were significantly different in the first attack of AP and CP. However, the significance disappeared after repetitive attacks (9 biomarkers after RAP2, 4 after RAP3 and 2 after RAP4+). RAP patients had an average of 3.07±1.85, whereas CP patients had 3.76±2.24 episodes of AP. In the CP registry, 98% of patients with CP had more than one acute episode, and the average number of attacks was 4-5 (4.07±3.82). The experimental

data revealed that the significant difference between inflammation-specific biomarkers (amylase, necrosis, edema, leukocyte infiltration) disappeared after 3 acute episodes.

Conclusion: Three or more attacks of AP with no morphological changes of the pancreas should be nominated as early CP.

Disclosure: Nothing to disclose

P1059

COMMON CASR VARIANTS IN HUNGARIAN CHRONIC PANCREATITIS PATIENTS

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Introduction: The calcium sensing receptor (CASR) has a pivotal role in maintaining mineral ion homeostasis and is also expressed in human pancreatic acinar and ductal cells. Over the past years, the possible involvement of common CASR variants in chronic pancreatitis (CP) has emerged, however, their role in the pathogenesis of CP remains controversial due to the lack of large case-control studies. We analyzed the clinically frequent CASR variants located in exon 7 in an ethnically homogenous group of Hungarian CP patients and healthy controls.

Aims & Methods: Our aim was to identify the common CASR polymorphisms in CP patients (cases) and controls with no pancreatic disease. We used PCR amplification and sequencing of the exon 7 with its flanking intronic regions. To further determine the role of two polymorphisms (p.A986S, p.R990G) we expanded our cohort and used the TaqMan™ SNP Genotyping Assays. Altogether, 261 cases and 489 controls were analyzed.

Results: We identified three common exon 7 variants in our cohort: c.2956G>T (p.A986S), c.2968A>G (p.R990G) and c.3031C>G (p.Q1011E). No significant differences were found in allele frequencies of these variants in cases compared to the control group: p.A986S (19.4% vs 17.2%, OR=1.16, p=0.3), p.R990G (7.9% vs 6.7%, OR=1.2, p=0.4) and p.Q1011E (3.6% vs 4.5%, OR=0.80, p=0.5). However, genotype distribution analysis revealed, that the p.A986S variant in homozygous state was overrepresented in patients relative to controls (3.5% vs 1.6%, OR=2.15, p=0.1).

Conclusion: The homozygous c.2956G>T (p.A986S) variant is overrepresented in the Hungarian cohort of chronic pancreatitis patients relative to the control group. Our results strengthen the previous findings in a French cohort (Masson E, 2015) and support the possible pathogenic role of the homozygous p.A986S variant in chronic pancreatitis.

Disclosure: Nothing to disclose

P1060

ENDOSCOPIC MANAGEMENT OF PANCREATIC DUCTAL LEAKS RESULTING IN PSEUDOCYSTS, FISTULAS, ASCITES AND EFFUSIONS IN CHRONIC PANCREATITIS WITHOUT USING CONTRAST IN ERP - OUR STUDY OF 321 CASES IN 11 YEARS- TRANSPAPILLARY OR TRANSMURAL MANAGEMENT?

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Introduction: Pseudocysts complicate chronic pancreatitis in around 10% of cases. Ductal disruptions is the cause rather than from peripancreatic pancreatic inflammation. There is always a ductal communication. Hence management strategies have to be different in management than in those after acute pancreatitis. These cysts hardly have any necrosis.

The mainstay of the management is diverting pancreatic fluid away from the leak to the small bowel with a pancreatic stent, allowing the leak to heal. Adjunct treatment includes medical therapy to decrease pancreatic exocrine secretions and salvage treatment with surgery. However, due to the low incidence of this condition, comparative studies with different treatment approaches are not available.

Aims & Methods: Aim: Management of pancreatic fistulas and pseudocysts in chronic pancreatitis. Transpapillary OR Transmural?

Methods: Selected all cases of chronic pancreatitis with pseudocysts, pleural effusions and pancreatic ascites, from 2008 October to 2019 December. Ascites and pleural effusions underwent therapeutic tapping. No pseudocysts were aspirated. MRCP performed. All put on intravenous antibiotics.

ERP was done, PD was attempted to be cannulated from the major papilla. If PD not be cannulated from major, minor papilla cannulation attempted. If we crossed the leak, a pancreatic sphincterotomy performed and 5Fr SPT stent placed. If wire did not cross leak and went into the cyst, a 5Fr DPT stent placed into the cyst.

No contrast used in ERP. Used fluoroscopy and terumo wire effectively.

In cases with no collections but only leak with wire not negotiated across the leak, 5Fr SPT stents placed reaching the area of leak. patients discharge in 4-5 days. Followed up after 3 months depending on their recovery and response.

If collections dry up, pancreatogram revealed normal duct, no further stenting. If dominant stricture, then stent exchange program with increasing diameter stents placed at interval of 6 months for a year and then a stent free trial given.

The 20 cases with failed cannulation, 12 were in the fistula group. 3 with leak responded after a prolonged medical management. 5 with distal leaks were subjected to distal pancreatectomy. 4 patients underwent a lateral pancreaticojejunostomy. 8 patients were treated using EUS Guided transmural drainage.

Results: ERP- 1324, Leaks 321/ 1324 (24.2%). In leaks, Ascites -60(18.7%), Effusions- 34(10.6%). Total 94. Of 94, 16(17.1%) collections. Pseudocysts - 227 (70.7%). ERP successful -301(93.7%). Failed - Total 20(6.2%) - 12 leaks & 8 pseudocysts.

94 leaks, 82(87.2%) technical success. Able to cross leak - 63(76.8%), Stents in collections- 7(8.5%).

Not crossed- 12(14.6%), Stents till leak 8(66.7%), EUS drainage - 4(33.3%). Site - jenu or proximal body-41(43.6%), Tail- 53(56.4%).

227 pseudocysts, 219(96.4%) treated transpapillary. Cysts drained -176(80.3%). Of these, stents in cysts- 133(75.6%).

Stents crossing leak 43 (24.4%). Of 43 - Infection 2(4.6%) requiring EUS aspiration. Resolution 14 (32.5%). EUS aspiration -non regressing

-19(44.1%), transmural drainage-8(18.6%). Site in pseudocysts- jenu & body 167(73.4%), tail 60(26.6%).

Pancreas divisum 24/ 321(7.5%).

ERP failed - 20(6.2%). 3(15%) managed medically, 5(25%) - distal pancreatectomy, 4(30%) - LPJ & Transmural drainage -8(20%).

Transmural drainage required in all 8 / 219(3.7%)

Conclusion: Pancreatic leaks and pseudocysts following chronic pancreatitis can be managed transpapillary in majority of cases. Transmural drainage when transpapillary fails.

Disclosure: Nothing to disclose

P1061 WITHDRAWN

P1062

PANCREATIC DISORDERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: FIRST RESULTS

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Introduction: Recently, much attention has been paid to the study of pancreatic disorders in patients with inflammatory bowel disease (IBD). According to literature in 20-30% of patients with IBD there is exocrine pancreatic insufficiency. Causes of pancreas pathology in IBD patients has been little studied. Possible etiological factors of relative cholelithiasis, drug damage (salazopyrine, steroids, azathioprine, metronidazole), hypercalcemia, hypercoagulation syndrome, smoking. In number of patients noted idiopathic or autoimmune pancreatitis.

Aims & Methods: To study the frequency and nature of pancreatic changes in patients with IBD.

105 patients with IBD were examined (53 men, 52 women), from there are 70 patients with ulcerative colitis (UC): 47% with total colitis, 53% with left-sided colitis, 35 patients with Crohn's disease (CD). Average age patients ranged from 18 to 75 years (mean: 33.5 years). Average disease duration 10 years (1-29). Pancreas involvement was assessed by the level of serum amylase and lipase, urine amylase, EPI in terms of fecal elastase - 1, standard examination methods were carried out, additionally CT or MRI of abdominal organs, endo-ultrasound and assessment of serum IgG4 level. Pain abdominal syndrome characteristic of pancreatitis was assessed by visual analog scale (VAS) from 0 to 10 points.

Results: Pain syndrome was noted in 39% of patients. Only 24.7% of patients revealed EPI (UC 27%, CD 20%), while severe EI occurred in 10% of patients with ulcerative colitis. The frequency of EPI in men and women was noted in approximately equal proportions: 53% to 47%, respectively, with UC, and with CD 57% and 43%. In 19% cases of EPI were observed in patients with a history of smoking and alcohol consumption, in 15% of overweight patients (average BMI 30.5). Structural changes in the pancreatic head were detected in 11.5% of patients. Convincing data for autoimmune pancreatitis have not been obtained in any of cases, although in 3 patients the level of IgG4 was increased 2.5 times, but this is not reliable confirmation of the diagnosis.

Conclusion: According to preliminary data, there is no clear relationship with the presence of exocrine insufficiency and disease severity, duration and the length of the lesion of the colon with ulcerative colitis and Crohn's disease. Exocrine insufficiency more often occurs at patients with a history

of alcohol consumption, smoking and overweight. No evidence of drug effects for the development of pancreatitis. Damage to the pancreas occurs in 24.7% of patients with IBD, moreover, characteristic for pancreatitis pain was observed in 41, and EPI in a quarter of patients. Frequency of involvement in the pathological process in men and women is the same in UC and in CD. Patients with autoimmune pancreatitis, against expectations, was not detected.

Disclosure: Nothing to disclose

P1063

CORRELATION BETWEEN THE PANCREATIC FIBROSIS AND PANCREATIC SECRETION IN PATIENTS WITH EARLY CHRONIC PANCREATITIS

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Introduction: Alteration of exocrine pancreatic function correlates with morphological damage in chronic pancreatitis (CP), mainly at advanced stages of the disease. It is also well known that as the degree of pancreatic fibrosis increases, the risk of exocrine pancreatic insufficiency increases as well.

However, correlation between morphological and functional changes at early stages of the disease has not been evaluated properly. The degree of pancreatic fibrosis in CP can be quantified by endoscopic ultrasound elastography (EUS-E), whereas pancreatic secretion can be accurately evaluated by the endoscopic pancreatic function test (ePFT).

Aims & Methods: Aim of the present study was to evaluate the correlation between the degree of pancreatic fibrosis and pancreatic secretion in patients with clinically and morphologically suspected early CP. Methods: Prospective, cross sectional and observational study. Patients with clinical suspicion of CP and 3-4 EUS criteria of the disease were included. EUS was performed with the slim Pentax Echoendoscope (EG-3270UK) and the HITACHI-Ascendus. Elastographic strain ratio (SR) was evaluated as the mean SR at the head, body and tail of the pancreas (normal <2.25). After that, 0.2µg/kg secretin was intravenously administered and bicarbonate concentration was measured in samples of duodenal juice collected at 15, 30 and 45 minutes after secretin (normal peak>80 mEq/L). Data are shown as mean±SD and percentages. Correlation between SR and bicarbonate peak was analysed by linear regression analysis.

Results: 62 patients were included (mean age 39.9 years, range 18-66, 22 female). Study could be completed in 61 patients. 39 patients (63.9%) presented 3 EUS criteria for CP, and 22 (36.1%) presented 4 criteria. Peak bicarbonate concentration was 63.8 ± 23.6 mEq/L, and it was abnormally low in 50 (81.9%) patients. SR was 3.85 ± 1.24 and it was abnormally high in all patients. Correlation between SR and bicarbonate secretion was highly significant ($r=0.715$, $p<0.0001$).

Conclusion: This study demonstrates a close correlation between pancreatic secretion and the degree of pancreatic fibrosis as evaluated by EUS-E in early CP.

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ic; Advisory Committees or Review Panels, Speaking and Teaching Mediglobe; Advisory Committees or Review Panels, Speaking and Teaching Abbott, Speaking and teaching Myland; Speaking and Teaching

P1064

PANCREATOSCOPY-GUIDED ELECTROHYDRAULIC LITHOTRIPSY FOR THE TREATMENT OF OBSTRUCTIVE DISTAL MAIN PANCREATIC DUCT STONES: A PROSPECTIVE CONSECUTIVE CASE SERIES (PELSTONE STUDY)

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Introduction: Pancreatoscopy-guided electrohydraulic lithotripsy (EHL) has shown potential in the treatment of patients with obstructive chronic calcifying pancreatitis (CCP), but is mostly used as second-line therapy after extracorporeal shockwave lithotripsy (ESWL). We aimed to investigate the efficacy and safety of pancreatoscopy-guided EHL as first-line therapy in patients with CCP of the distal main pancreatic duct (PD).

Aims & Methods: A prospective single center consecutive case series was performed in CCP patients presenting with obstructing stones of >5mm in the head or the neck of the pancreas. Stone fragmentation was carried out using EHL. The primary study outcome was technical success defined as the ability to visualize the intraductal stones and achieve stone fragmentation, complete (100%) or partial (≥50%), with resolution of PD outflow obstruction (indicated by the passage of a balloon). Secondary outcomes were clinical success (Izbicki pain score), adverse events, and number of interventions.

Results: For this study, 33 consecutive patients were considered. Pancreatoscopy was not performed due to failure to cannulate the PD (n=5) or the observation that stones were already fragmented after a PD stent was placed at the initial ERP procedure (n=3). In patients in whom pancreatoscopy was attempted, technical success was achieved in 24 out of 25 patients (96%). Complete stone clearance was achieved in 19 patients (79.2%) and partial in 5 patients (20.8%). In one patient the procedure failed because the EHL probe could not be positioned in front of the stone. Median stone size was 8 mm (IQR 3). A median of 1 (IQR 0.46) intraductal stone was present. PD clearance was achieved after a median of 2 (IQR 2) ERP procedures and 1 (IQR 1) EHL procedure. In 13 patients (54.2%) a stent was placed prior to EHL performance to facilitate pancreatoscopy at a second ERP. The mean Izbicki pain score at baseline was 62.4 ± 21.6 (n=24/24). After 1, 3 and 6 months of follow-up it dropped significantly to 33.4 ± 26.1 (n=16/23), 15.9 ± 17.7 (n=19/22) and 22.3 ± 30.3 (15/18), respectively ($p=0.006$). Adverse events included post-ERCP pancreatitis (n=8) and cholangitis (n=1). All were mild and treated conservatively.

Conclusion: Pancreatoscopy-guided EHL is a highly effective treatment for symptomatic CCP patients with a dilated PD due to obstructive PD stones in the pancreatic head or neck. Adverse events, mainly pancreatitis, occur relatively frequent, but are mild. Future studies should focus on the implementation and cost-effectiveness of EHL as a first-line treatment strategy in daily clinical practice.

Disclosure: Investigator initiated study financed by Boston Scientific Inc.

P1065

ETIOLOGY AND NATURAL COURSE OF CHRONIC PANCREATITIS

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Introduction: Chronic pancreatitis (CP) is a complex disease with a substantial burden on patients and their caregivers. Data on epidemiology and natural course of CP mostly rely on registry-based study designs. Scarce longitudinal studies with real-patient cohorts are usually small, due to difficult early diagnosis, variable progression from acute to CP and a challenging follow up of the patients (the majority is noncompliant with history of alcohol consumption and smoking). In particular, differences in long-term outcomes between various etiologies of CP represent a significant knowledge gap.

Aims & Methods: To determine outcomes of CP in relation to different etiologies in a high-volume tertiary centre.

We retrospectively analysed prospectively collected data from electronic medical charts of all consecutive patients with CP, treated at Pancreatic Outpatient Clinic of Karolinska University Hospital in Stockholm, Sweden. Etiology of CP was determined according to M-ANNHEIM classification system, and only patients with a definite diagnosis of CP were included. Final analysis was further restricted to patients who received a definite diagnosis of CP between 2003 and 2018, and for whom etiology was available.

Results: In total, 549 patients (352 male and 197 female) were included in the analysis. Median age was 56 years at the time of CP diagnosis. Etiology was distributed as follows: alcohol and nicotine (40.4%), nicotine only (16.2%), efferent duct factors (11.3%), immunological factors (11.3%), alcohol only (8.9%), hereditary (6.9%) and miscellaneous/nutritional/other/combination of etiologies in 4.9%. Only 7.5% of patients had a positive family history of pancreatic disease. Prior episode of acute pancreatitis (AP) was documented in 357 (65.0%) subjects, of whom 252 (70.6%) progressed to recurrent AP. There was no significance in prevalence of calcifications, diabetes mellitus (DM) or pancreatic exocrine insufficiency (PEI) among patients with alcohol intake, nicotine only or a combination of both. However, the frequency of calcifications and diabetes was significantly higher in these patients comparing to other etiological groups ($p < 0.0001$ and $p = 0.07$, respectively). PEI was most common in patients with immunological etiology of CP ($p = 0.002$). Nearly half of all subjects (45.5%) underwent ERCP, predominantly for obstruction and pain treatment. Surgery was performed in 127 (23.1%) patients, mostly due to suspicion of cancer, disease progression and pain. After a median observation time of 5.2 years (range 0 to 16.9 years), 149 (27.1%) patients died. Overall survival was significantly better for patients with hereditary and immunologic CP, but it was similar for patients who consumed alcohol, nicotine only, a combination of both and efferent duct CP.

Conclusion: CP is the most common in individuals with a history of alcohol and nicotine consumption. Prevalence of DM, calcifications and PEI was not significantly different between patients with alcohol intake, smoking only or a combination of both. However, comparing to other etiological factors, calcifications and DM are significantly more prevalent in patients who smoke and/or drink. After a median follow-up time of 5.2 years, 27.1

% of patients died. Overall survival is significantly better for patients with hereditary and immunologic CP, but it is similar for patients who consumed alcohol, nicotine only, a combination of both and efferent duct CP.

Disclosure: Nothing to disclose

P1066

STRUCTURAL PANCREATIC CHANGES ARE RELATED TO RISK FACTORS IN CHRONIC PANCREATITIS - A MULTIVARIATE ANALYSIS MODEL FROM THE SCANDINAVIAN BALTIC PANCREATIC CLUB (SBPC) IMAGING DATABASE

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Introduction: The Scandinavian Baltic Pancreatic Club prospectively includes patients with definite or probable chronic pancreatitis (CP) according to the M-ANNHEIM diagnostic criteria. Demographic data, etiological factors and pancreatic imaging assessments are registered.

Aims & Methods: In this retrospective, cross-sectional observational study, we assessed the associations between etiological and time factors for CP (smoking, alcohol abuse, recurrent acute pancreatitis, age and disease duration), and structural pancreatic changes in a standardized and validated CP imaging assessment system. Assessments were analyzed by binary logistic regression.

We aimed to validate a multivariate model describing the association between etiological factors and structural pancreatic changes in CP.

Results: We included 959 patients (66% males, mean age (SD) 55 (14) years. We detected structural pancreatic changes in 94% of the subjects: 66% had calcifications, 59 % main pancreatic duct dilatation and 22% pancreatic atrophy. Smoking history was associated to calcifications in the multivariate analysis; OR; 1.76 (95% CI, 1.13, 2.74). Current alcohol abuse was associated to pseudo-cysts; OR; 2.05 (95% CI, 1.23, 3.44). Cumulated heavy drinking did not associate with a specific pattern of structural pancreatic changes. Long disease duration was associated with higher prevalence of calcifications; OR; 1.71 (95% CI, 1.10, 2.66) and pancreatic atrophy; OR; 2.43 (95% CI, 1.43, 4.12).

Conclusion: Etiological factors and disease progression associate to structural pancreatic changes in CP. We conclude from this large scale study, using a multivariate model taking the influence of several risk factors into account, that etiological factors and disease duration are associated to specific patterns of structural pancreatic changes in CP.

Disclosure: Nothing to disclose

P1067

PREVALENCE OF PANCREATIC PARENCHYMAL ABNORMALITIES AND CHRONIC PANCREATITIS IN PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS UNDERGOING LIVER TRANSPLANTATION

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Introduction: Concurrence of alcoholic liver cirrhosis (ALC) and alcoholic chronic pancreatitis (ACP) is rare, although both conditions share the same environmental risk factors. The aim of our study was to investigate the prevalence of parenchymal abnormalities of the pancreas and the prevalence of chronic pancreatitis in patients undergoing liver transplantation for alcoholic cirrhosis of the liver.

Aims & Methods: We performed a retrospective analysis of radiological reports and medical records of all adult patients who had undergone liver transplantation for ALC at our center between October 1995 and October 2019.

Parenchymal abnormalities of the pancreas were assessed by pre-transplant CT and were classified as (1) atrophy, (2) calcification, (3) cystic lesion/s, (4) lipomatosis and (5) combination of two or more features.

Results: Four hundred and ninety-five orthotopic liver transplantations were performed in 387 males and 108 females (average age 56.5 ± 8.4 years at the time of the procedure). The indication for transplantation was liver cirrhosis caused by chronic alcohol abuse (in some patients in combination with viral hepatitis) or hepatocellular cancer in alcoholic liver cirrhosis. Sixteen of these patients (3.4%) had diagnosis of alcoholic chronic pancreatitis. Parenchymal abnormalities on CT were reported in 77 patients (15.6%); atrophy of the gland was found in 29 of them (37.7%), calcification without other pathology in 3 patients (3.9%), cystic lesions in 12 patients (15.6%), pancreatic lipomatosis in 14 patients (18.2%) and combination of two or more features in 19 patients (24.7%).

Conclusion: In our cohort, the co-occurrence of ALC and ACP was rare (3.4%). However, parenchymal abnormalities on CT were found in nearly 16% of patients with ALC, with pancreatic atrophy being the most commonly reported. This observation emphasizes the importance of combining clinical, imaging and functional criteria in diagnosing chronic pancreatitis.

Disclosure: Nothing to disclose

P1068

PATOGENETIC MECHANISMS OF PANCREATOGENIC DIABETES: PRELIMINARY RESULTS

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Introduction: There are still doubts about relationship between chronic pancreatitis and diabetes mellitus. There is limited data concerning mechanisms of pancreatogenic diabetes occurrence and pathogenesis.

Aims & Methods: The aim of the study was to identify the pathogenetic differences between diabetes mellitus on the background of chronic pancreatitis (CP+DM) and type 2 diabetes (type 2 DM) by defining of incretins level.

A total of 66 patients were enrolled in the study, they were divided in to three groups: 40 patients were with chronic pancreatitis (CP) (male:female = 25:15, average age was 52±11.5 years), 11 patients were with CP+DM

(male :female = 6:5) and 11 patients were with type 2 DM (male:female = 6:5), groups were comparable by age. The control group included 25 persons; average age was 33.2±8.6 years.

The incretin levels (gastro-inhibiting polypeptide (GIP) and glucagon-like peptide-1 (GLP-1)) were determined in fasting blood and 10 minutes after a breakfast by ELISA. Body mass index (BMI) and insulin resistance index (HOMA-IR) were taken into account as well.

Results: BMI was the same (24±2.5 kg/m²) in groups of patients with CP and CP+DM. BMI was significantly higher (35±3.2 kg/m²) in patients with type 2 DM compared to the above groups, in the control group BMI was 24±0.5 kg/m². HOMA-IR was 2.0±1.8; 2.3±1.9; 1.9±0.7 in groups of CP, CP+DM and control group, respectively, that matched normal values. At the same time HOMA-IR was significantly higher in patients with type 2 DM (4.8±3.5) than in patients from previous groups, p< 0.05.

Thus, overweight and insulin resistance were not observed in patients with CP and CP+DM, in contrast to patients with type 2 DM.

GIP levels were 22.90±3.9 pg/ml and 45.0±3.4 pg/ml, before and after a breakfast, respectively, in the control group. In case of patients with CP fasting GIP level was 30.9±9.0 pg/ml, after a breakfast it rose up to 68.0±17.0 pg/ml. Fasting GIP level was 34.0±7.0 pg/ml, after a breakfast it was 40.0±4.5 pg/ml in group of patients with CP+DM, remarkable that there was not physiological recovery of incretin level in this group of patients. However, physiological recovery of GIP was observed in the type 2 DM group, where GIP level was 41.0±19.0 pg/ml and 70.0±16.0 pg/ml, before and after a breakfast, respectively. No significant differences in GLP levels between all groups were found.

Conclusion: No increase of GIP level after a meal in patients with diabetes mellitus on the background of chronic pancreatitis in the presence of normal body mass index and normal values of HOMA-IR proves the existence of pancreatogenic (type 3c) diabetes and demonstrates the presence of pathogenetic difference between diabetes mellitus on the background of chronic pancreatitis and type 2 DM.

Disclosure: Nothing to disclose

P1069

IS ABDOMINAL PAIN OVERESTIMATED IN CHRONIC PANCREATITIS? - CLINICAL DATA FROM A PORTUGUESE REFERENCE CENTER

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Introduction: Abdominal pain has been referred as a frequent feature and major complication of chronic pancreatitis (CP) with a difficult approach in clinical practice.

Aims & Methods: The aim of this study is to evaluate its frequency in a cohort of patients with CP and the predictive factors for chronic pain in this entity.

A unicentric retrospective cohort study of CP patients followed in a hospital between January/2010 and December/2017. Patients with abdominal chronic pain and its risk factors were evaluated. Statistical analysis was performed with SPSS software version 26 (Mann-Whitney tests and Fisher's exact test). A p-value ≤ 0.05 was considered statistically significant.

Results: We included 92 patients with CP. 38% (n = 35) presented with exacerbations, but only 7,6% (n = 7) had abdominal chronic pain. Data for each risk factor will be presented with the % related to the patients with

pain in the first place. Sex (male 71.4% versus 85.9%; female 28.6% versus 14.1%; p-value: 0.288) and age (average of 53 years versus 63 years; p-value: 0.089) did not proved to be predictive factors for the occurrence of pain. The etiology of CP was also not a risk factor (85.7% alcoholic etiology versus 83.7%; 14.3% idiopathic versus 11.8%; p-value: 1.0). There was no statistical association with other factors, such as smoking habits (71.4% versus 58.8%; p-value: 0.698); alcohol intake (85.7% versus 88.2%; p-value: 1.0) or diabetes mellitus (28.6% versus 56.5%; p-value: 0.24). Nor with structural findings, such as inflammatory masses or fluid collections (p-value: 0.196 and 1.0, respectively), groove pancreatitis (p-value: 0.076), bile duct (p-value: 0.361) or pancreatic duct (p-value: 0.361) stricture, neither with bile duct (p-value: 1.0) or pancreatic duct (p-value: 0.34) stones. 28.6% of patients with pain underwent surgery versus 12.9%, with no statistical significance (p-value: 0.26). Mortality rate of 14.3% versus 25.9%, with no statistical significance (p-value: 0.675).

Conclusion: In our study only a small percentage of patients had chronic abdominal pain as a clinical manifestation of CP and we didn't find any risk factor for its occurrence.

Disclosure: Nothing to disclose

P1070

CHRONIC PANCREATITIS - EPIDEMIOLOGICAL AND CLINICAL CHARACTERIZATION OF A COHORT OF PATIENTS FROM A PORTUGUESE REFERENCE CENTER

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Introduction: The epidemiological data on chronic pancreatitis (CP) in Portugal is scarce due to the difficulty in early diagnosis and the variable clinical progression from acute to CP.

Aims & Methods: The aim of this study is to present a real-life cohort of patients with CP from a Portuguese reference center.

Data collected retrospectively from a prospective database of patients with CP of a reference center between january/2010 and december/2017. CP was defined by clinical and structural features consistent with irreversible pancreatic inflammation. Demographic characteristics, imaging modalities and clinical features complications were evaluated.

Results: 92 patients, 84.9% men, mean age 61.4 years (38-87). Alcoholic pancreatitis was the most common form of pancreatitis (83.7%, n=77), followed by idiopathic/under investigation (11.9%, n=11), autoimmune (2.2%, n=2), acute recurrent pancreatitis (1.1%, n=1) and obstructive (1.1%, n=1). Smoking intake was documented in 55 patients (59.8%). 50 subjects had diabetes mellitus (54.3%) and 7 presented with chronic abdominal pain (7.6%).

The most common complications were pseudocysts (n=20). 65.2% (n=60) underwent abdominal ultrasound and the most common findings were: Wirsung dilation (n=37), heterogeneous pancreas (n=33) and calcifications (n=30). 92.4% (n=85) performed abdominal computed tomography and the most common findings were: calcifications (n=58), Wirsung dilation (n=55) and atrophic pancreas (n=37).

Magnetic resonance with or without cholangiopancreatography was performed in 45.7% of the patients (n=42) and the most common findings were: dilation of the Wirsung (n=25), atrophic pancreas (n=20) and bile ducts dilation (n=11). 50% (n=46) underwent cholangiopancreatography: common bile duct stenosis (n=22), Wirsung (n=15) and common bile duct dilations (n=12) were the most prevalent findings.

Endoscopic ultrasound was made in 33.7% of the patients (n=31), which most frequent findings were Wirsung dilation (n=14), heterogeneous pancreas (n=14) and calcifications (n=13).

3.3% (n=3) developed pancreatic neoplasia. 40.2% (n=37) underwent endoscopic therapy and 14.1% (n=13) were submitted to surgery. The mortality rate during follow-up was 25% (n=23, 3/23: pancreatic neoplasia, 20/23: not related to CP).

Conclusion: We present a cohort with a significant number of patients that addresses the diagnostic and clinical challenges of this entity. The difficulty of therapeutic options and risk of complications should prompt close follow-up.

Disclosure: Nothing to disclose

P1071

DIAGNOSTIC YIELD OF FECAL ELASTASE TESTING IN CLINICALLY SUSPECTED EXOCRINE PANCREATIC INSUFFICIENCY

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Introduction: Exocrine pancreatic insufficiency (EPI) is characterized by reduced or a inadequate secretion or activity of pancreatic juice and its enzymes. Clinically, its spectrum varies from recurrent abdominal pain and bloating to overt malabsorption. EPI is frequently a consequence of pancreatic disease, but it can also occur in extrapancreatic conditions. Early recognition of EPI is important in order to avoid nutritional complications and improve quality of life of patients. Our aim was to assess the diagnostic yield of fecal elastase-1 (FE-1) in patients with clinically suspected EPI.

Aims & Methods: We recruited all patients with clinically suspected EPI in whom FE dosing was done as part of their diagnostic workup. Baseline assessment consisted of demographic data, full history (including alcohol, smoking and family history), recording stool frequency, clinical examination, laboratory parameters and imaging data. Also details on final diagnosis were collected on follow-up. FE is the most commonly indirect test used for quantifying the exocrine pancreatic function. We measured the FE-1 concentration with an enzyme linked immunosorbent assay (ELISA) kit.

Results: We included 140 patients from our Gastroenterology Unit over a period of 6 months, with mean age of 53 ± 3 years, 68% male. We divided them in 2 groups: group A with a normal FE-1 (>200 ug/g stool) and group B with low FE-1 (< 200 ug/g stool).

Group A represented 74% and group B 26% of the patients. Mean age of patients with low FE-1 was 56 ± 2 years, with a distribution of 44% (16) female and 56% (20) male. Group A had a slight female predominance of 54% (56), with the remaining 46% (48) being male. With regard to smoking and alcohol consumption, the percentage of smokers in the cohort was 42% and 41% reported history of alcohol use. From all the patients with increased stool frequency, low FE-1 was seen in 33% of them, and from all the patients with abdominal pain 29% had EPI as defined by a decreased FE-1. In patients with weight loss, 52% had low values of FE-1. Overall in the group with a low FE-1 we identified 33 patients with chronic pancreatitis, 2 with an inflammatory bowel disease (IBD) and 1 had autoimmune pancreatitis. Also diabetes was more frequent in patients with EPI (25% vs 14.4%).

Conclusion: Weight loss, but also increased stool frequency can be associated with EPI and should prompt for FE-1 testing in the diagnostic work-up, especially in diabetic patients or with risk factors. Because EPI can lead to impaired quality of life we have to consider all this puzzle pieces.

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Disclosure: Nothing to disclose

P1072 WITHDRAWN

P1073

SPECIFIC FEATURES OF ENDOSCOPIC ULTRASOUND WITH CONTRAST-ENHANCEMENT AND ELASTOGRAPHY ALLOW THE DIFFERENTIAL DIAGNOSIS BETWEEN FOCAL AUTOIMMUNE PANCREATITIS AND PANCREATIC ADENOCARCINOMA

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Introduction: The differential diagnosis between focal autoimmune pancreatitis (AIP) and pancreatic cancer (PC), can be very challenging. Endoscopic ultrasound (EUS) may provide information useful. However, the specific EUS features associated with AIP diagnosis have been poorly investigated.

Aims & Methods: The aim of this study is to investigate EUS features associated with focal AIP diagnosis. Data on patients with AIP underwent EUS between May 2008 and February 2020 were retrospectively collected. Only type 1 AIP patients with focal pancreatic enlargement were evaluated. Clinical and EUS features of this group were compared with a control group of patients with a histologically confirmed PC. The subsequent EUS features were evaluated: parenchymal features (focal mass echogenicity-FE, loss of lobularity-LL, distal atrophy-DA, peripancreatic hypoechoic margins-PHM), features of pancreatic duct (PD) / common bile duct (CBD) (PD dilation-PDD, PD stenosis-PDS, thickening of PD/CBD walls- PD/CBD-TW) and peripancreatic features (lymphadenopathies-LN and vessel infiltration-VI). Also, contrast-enhanced EUS (CE-EUS) and elastography features were recorded.

Results: We recruited 50 patients with AIP and 36 with PC (in all these cases the indication to EUS was suspect of pancreatic tumor). After the application of inclusion/exclusion criteria 14 patients with focal type 1 AIP were included. From an epidemiological and clinical point of view, sex distribution and onset of symptoms were significantly different between the two

groups, with a higher prevalence of male sex (85.7 vs 50%, $p=0.002$) and jaundice (64.3 vs 36.1%, $p=0.008$) in AIP. On EUS FE was hypoechoic in both groups in 100% of cases. DA was observed more frequently in PC ($p=0.06$). On elastography the mass was rigid in 96.6% of PC and in 33.3% of AIP ($p<0.001$), while on CE-EUS there was a hypo-enhancement respectively in 97.2 and 25% ($p<0.001$). VI was suspected in 21.4% of AIPs and 88.9% of PCs ($p<0.001$). A significant difference was found also in presence of PHM, in PDS, PDD, PD-TW and CBD-TW.

Conclusion: AIP and PC have different and peculiar endosonographic features that permit to distinguish these two diseases. Contrast behavior, elastography, thickening and dilation of ducts, mass echogenicity and vessels infiltration should be carefully evaluated and described in patients with pancreatic focal mass.

Disclosure: Nothing to disclose

P1074

LONG TERM RESPONSE TO RITUXIMAB IN PATIENTS WITH TYPE 1 AUTOIMMUNE PANCREATITIS

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Introduction: Autoimmune pancreatitis (AIP) is an independent entity of chronic pancreatitis. It comprises both IgG4-related disease (IgG4-RD) and Type 2 Autoimmune Pancreatitis (type 2 AIP). To date, steroid therapy represents first line treatment in both subtypes, but due to a high relapse rate in patients with IgG4-RD Rituximab (RTX), by depleting B-lymphocytes, seems to be safe and efficient as a maintenance therapy.

Aims & Methods: The aim of the study was to evaluate long term effects of Rituximab in IgG4-RD.

We included AIP patients from our clinic with diagnosed AIP between June 2006 and August 2019. Patients were excluded if International Consensus Diagnostic Criteria or Unifying-AIP criteria were not fulfilled or the clinical suspicion was unspecific.

Results: In total, 69 patients were included (IgG4-RD $n=46$, Type 2 AIP $n=23$) with a median follow up of 35 months (range 0-60). Due to therapeutic failure under steroids 13 out of 46 patients with IgG4-RD were treated with RTX. In a subgroup of patients with no sufficient steroid response we observed a beneficial effect from a therapy with RTX: After RTX treatment the reduction of the Response Index was significant and within the range of patients that have already shown a sufficient response to steroids.

IgG4 serum levels were measured before and after RTX and declined along with clinical response. After 10 months we observed a clinical relapse in 50% of our patients. In a multivariate analysis we found no risk factors (smoking, intestinal bowel disease, number of involved organs, endocrine or exocrine insufficiency or IgG4 levels) correlating with the Response Index or the relapse-free survival.

Conclusion: The usage of a Response Index is reasonable to assess the activity of disease for identifying patients who benefit from a B-cell depletion. Rituximab as a maintenance therapy in patients with IgG4-RD is an effective treatment with long term effects, but repetitive administration after 6 months might reduce the risk of relapse.

Disclosure: Nothing to disclose

P1075

DIABETES MELLITUS IS A RISK FACTOR FOR PANCREATIC DUCTAL ADENOCARCINOMA IN PATIENTS WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM

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Introduction: Patients with pancreatic cyst, especially intraductal papillary mucinous neoplasm (IPMN), are likely to develop pancreatic ductal adenocarcinoma (PC) at another site. Therefore, it is important to check for PC while observing patients with IPMN.

Aims & Methods: In this study, we considered cases with IPMN following the involvement of PC, and studied risk factors for induction of PC. We reviewed 385 patients (median age: 71 (35-93), M:F = 149:236) with IPMN who were diagnosed at our institute between 2004 to 2017 and followed with imaging examinations. We excluded IPMNs appropriate for surgery at first visit to our institute. The breakdown of the patients was 283 with IPMN and 102 with IPMN plus non-IPMN/serous cystic neoplasm (SCN) cyst. The median cyst diameter was 15.5 mm (5-68), the main pancreatic duct caliber was 2.5 mm (1-9.5), and 253 patients had multiple cysts. In many cases, patients were examined twice a year using computed tomography (CT) or magnetic resonance cholangiopancreatography (MRCP). The median observation time for a cystic lesion was 54 months (12-172). We studied details of patients that developed PC and performed statistical analysis to determine risk factors for cancer in patients with pancreatic cyst.

Results: Due to a worsening condition from the cyst, 8 patients underwent further therapy. The results were 1 SCN, 3 intraductal papillary mucinous adenoma, and 4 intraductal papillary mucinous adenocarcinoma (IPMC) as carcinoma *in situ* (CIS). There were no deaths associated with a cystic lesion. In contrast, invasive PC developed in 10 patients (10/385, 2.6%) at a different site from the IPMN. The median time from cyst detection to PC development was 41 months (13-128) and median age of PC development was 76 years old (60-86). Stages (UICC) were 6 in 2a, 3 in 2b, and 1 in 4 and the median survival period was 1,444 days.

These unsatisfactory results may indicate that our following method was inadequate. In univariate analysis to search for risk factors for developing PC to IPMN, diabetes mellitus (DM) at the time of cyst detection (DM: non-DM = 7/74 (9.5%): 3/301(1.0%), $P < 0.001$) was significant. In multivariate analysis, DM was significantly associated with PC development ($P < 0.01$).

Conclusion: In this study, PC developed in 10 patients (2.6%) during the observation period and their prognosis was worse than 8 patients that underwent therapy due to a worsening of the cyst. Therefore, careful observation for PC development is necessary. It might be necessary to use endoscopic ultrasonography for observation and to shorten the examination interval for at-risk patients with DM.

Disclosure: Nothing to disclose

P1076

PANCREATIC AND HEPATOBILIARY MANIFESTATIONS OF FATTY PANCREAS: A REFERRAL MULTI-CENTER EXPERIENCE

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Introduction: Fatty Pancreas (FP) is an increasingly encountered disease with an accumulating evidence of association with numerous co-morbidities including obesity, metabolic syndrome and non-alcoholic fatty liver disease. However, data regarding linkage between FP and other pancreatic and hepato-biliary disorders are still accumulating.

Aims & Methods: We aimed to investigate the association of pancreatico-hepato-biliary disorders with FP. All patients who underwent endoscopic ultrasound (EUS) for hepatobiliary indications at two referral Israeli medical centers from 1st January 2018 to 1st January 2020 and for whom the endosonographer reported on the presence or absence of FP were retrospectively analyzed.

Results: Overall, 569 patients were included in the study. Seventy-eight patients (13.7%) had FP (group A) as compared to 491 patients (86.3%) who didn't have FP (group B). The average age in group A was 62.1 ± 14.1 vs. 62.9 ± 14.1 in group B. FP was significantly associated with obesity (OR 4.98, 95% CI 3.02-8.24, $P < 0.0001$), Hypertension (OR 2.55, 95% CI 1.57-4.15, $P = 0.0002$), active smoking (OR 2.02, 95% CI 1.04-3.93, $P = 0.03$) and hyperlipidemia (OR 2.86, 95% CI 1.58-5.18, $P = 0.0005$).

On multivariate regression analysis: fatty liver (OR 5.49, 95% CI 2.88-10.49, $P < 0.0001$), main duct intraductal papillary mucinous neoplasm (M-IPMN) (OR 2.69, 95% CI 1.05-6.9, $P = 0.04$) and gallbladder stones (OR=1.93, 95%CI 1.1-3.38, $P = 0.02$) were the most endoscopic ultra-sonographic diseases that significantly correlated with FP with ROC of 0.722.

Conclusion: FP was associated with several diseases, most importantly the premalignant M-IPMN. Investigation for these coexistent diseases should be considered while FP is encountered.

Disclosure: Nothing to disclose

P1077

THE UTILITY OF ENDOSCOPIC ULTRASOUND FINE NEEDLE ASPIRATION IN PANCREATIC CYSTIC LESIONS DIAGNOSIS

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Introduction: The diagnosis of pancreatic cysts is mainly based on imaging and biochemical cyst fluid analysis obtained via fine needle aspiration (FNA), because of low yield of cytology. However, the utility of FNA is still unknown as biochemical fluid analysis has wide sensitivity and specificity.

Aims & Methods: We aimed to assess whether biochemical cyst fluid analysis correlate with the endoscopic ultra-sonographic (EUS) diagnosis based on morphological cyst properties. A retrospective study including patients who underwent EUS-FNA in Galilee Medical Center was performed. Agreement level between EUS diagnosis and biochemical analysis was reported.

Results: One-hundred and eleven patients were included. For cyst CEA level, 42.4% of patients with endoscopic diagnosis of pancreatic mucinous cystic neoplasm (IPMN and MCN) had CEA level > 192 ng/mL as defined in the literature vs. 15.8% of patients who had another endoscopic diagnosis (chi square 0.03). The agreement level with CEA > 192 ng/mL was poor (Kappa correlation =0.130). For the serous cystadenoma (SCA) patients, the level of amylase and CEA was defined as < 250 unit/L and < 5 ng/mL, respectively. Eight patients (57.1%) had amylase of < 250 unit/L, while 42.9% had > 250 unit/L (chi square 0.007). The agreement level between EUS diagnosis of SCA and amylase level was poor (Kappa correlation =0.231). For cyst CEA level, 71.4% had CEA level < 5 ng/mL vs. 28.6% who had CEA > 5 ng/mL (chi square < 0.001) with fair agreement level (Kappa correlation =0.495).

Conclusion: EUS-FNA for pancreatic cystic lesions poorly correlated with the endoscopic sonographic diagnosis. FNA should be considered in the setting of worrisome findings.

Disclosure: Nothing to disclose

P1078

THE YIELD OF STRING SIGN IN DIFFERENTIATING MUCINOUS FROM NON-MUCINOUS PANCREATIC CYSTS: A CROSS-SECTIONAL STUDY

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Introduction: The diagnosis of pancreatic cystic neoplasms is often complicated and depends on several diagnostic modalities, including imaging, cyst fluid biochemical analysis and cytology.

Aims & Methods: The aim of our study is to assess the performance of string sign in differentiating mucinous from non-mucinous pancreatic cysts. A retrospective study including patients who underwent EUS-FNA for investigation of pancreatic cysts with reporting the string sign in Galilee Medical Center was performed.

Results: One-hundred and twelve patients were included in the study. Ninety-two patients (82.1%) diagnosed with mucinous cystic neoplasms (group A) vs. 20 patients (17.9%) diagnosed with non-mucinous (group B). The average age in groups A and B was 71.3 and 60.4 years, respectively. String sign was negative in 21 patients (22.8%) and positive in 47 patients (51.1%) in group A, while in group B, string sign was negative in 19 patients (95%). String sign showed significant correlation with the diagnosis of mucinous cystic neoplasms (OR 42.5, 95% CI 5.3-339, P=0.0004). In the cytology confirmed mucinous cystic neoplasms that included 32 patients, the sensitivity, specificity, PPV and NPV of string sign with mucinous cystic neoplasms were high and reached 91.7%, 87.5%, 95.7% and 77.8%, respectively with excellent accuracy rate of 90.6%.

Conclusion: The string sign is highly accurate for predicting pancreatic mucinous cystic neoplasms, this sign should be used as an important aid for improving diagnostic accuracy.

Disclosure: Nothing to disclose

P1079

KRAS/GNAS-TESTING BY DEEP TARGETED NGS IMPROVES THE EUS-GUIDED WORKUP OF SUSPECTED MUCINOUS NEOPLASMS OF THE PANCREAS

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Introduction: Pancreatic cysts or dilated pancreatic ducts are often found by cross-sectional imaging, but only mucinous lesions can become malignant. Therefore, distinction between mucinous and non-mucinous lesions is crucial for adequate patient management.

Aims & Methods: We performed a prospective study including targeted NGS of cell-free DNA in the diagnostic EUS-guided workup. Pancreatic cyst(s) or main duct fluid obtained by EUS-guided FNA was analysed by CEA, cytology and deep targeted NGS of 14 known gastrointestinal cancer genes with a limit of detection down to variant allele frequency of 0.01%. Results were correlated to histopathology and clinical follow-up.

Results: 93 patients with pancreatic cyst(s) and/or a dilated pancreatic main duct (≥5 mm) were screened. 51 patients had to be excluded, mainly due to inoperability or small cyst size (≤ 10 mm). 42 patients were enrolled for further analysis. A final diagnosis was available in 24 cases including 7 negative controls. In 37/42 (88.1%) of patients a KRAS- and/or GNAS-mutation was diagnosed by NGS. 30.0% of the KRAS-mutated and 11.8% of the GNAS-mutated lesions harbored multiple mutations. KRAS/GNAS-mutations were detected in all histologically proven mucinous neoplasms but in none of the non-mucinous lesions. KRAS/GNAS-testing by NGS, cytology, and CEA had a sensitivity and specificity of 100% / 100%, 50% / 100% and 58.3% / 85.7%, respectively. Tests were discordant in 11/24 (45.8%).

Conclusion: KRAS/GNAS-testing by deep targeted NGS is a suitable method to distinguish mucinous from non-mucinous pancreatic lesions, suggesting its usage as a single diagnostic test. Results must be confirmed in a larger cohort.

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Disclosure: Nothing to disclose

P1080

SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES ON BD-IPMN MALIGNANCY PROGRESSION

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Introduction: Despite the low risk of malignancy of branch-duct IPMN (BD-IPMN) this subtype of cystic lesion of the pancreas represents a potential precursor lesion of pancreatic carcinoma. Risk of malignancy of BD-IPMN during the follow-up range between 3% to 8% in published series. Therefore, the majority of patient are referred to a surveillance program, while surgery is considered only for those patients developing features of degeneration or malignancy during the follow-up.

Aims & Methods: A comprehensive research was conducted on PubMed, Cochrane and Embase for observational studies focused on BD-IPMN risk of malignancy progression published before January 1st, 2020.

Results: Twenty-four studies were included for a total of 8941 patients enrolled. Data collected from the studies showed that 20.2% of patients with BD-IPMN had a progression and 11.8% underwent surgery. From the surgical cohort, 23.6% had a malignancy at the final anatomopathological examination and 34.3% had a PDAC. The 0.6% had a distant malignancy and the mortality rate was 1.16%. A meta-analysis was conducted in order to assess the best treatment for BD-IPMN patients.

Conclusion: According to the available data, there is no reason to dismiss patients during the follow-up (unless they are no more fit for surgery). In the light of international guidelines, more data should be collected in order to assess the best timing for the follow-up intervals and surgery in patients with BD-IPMN.

Disclosure: Nothing to disclose

P1081

PROGRESSION OF CYSTIC PANCREATIC NEOPLASMS: A UNI-CENTER COHORT STUDY OVER 6 YEARS

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Introduction: The purpose of this study was to evaluate the malignant potential of pancreatic cystic lesions and the precision of endosonographic diagnoses including the early detection of cysts with malignant potential.

Aims & Methods: All patients referred between January 2012 and December 2018 to our tertiary referral center for EUS of pancreatic cystic lesions were included in this retrospective analysis. EUS was performed by 3 experienced gastroenterologists with Hitachi Preirus and Pentax echoendoscopes.

Results: 455 patients with pancreatic cystic lesions were included in a database. 223 patients had cystic pancreatic neoplasms, the median age was 69.0 years. EUS diagnosis was 138 BD-IPMN, 16 MD-IPMN, 46 serous cystic neoplasia and 6 mucinous cystic neoplasia. Progression of size was rare. In 52 BD-IPMN with more than one examination only 6 lesions showed increase of ≥ 2 mm. In 29 cases, a histopathological diagnosis was available after surgical resection. 25.0% of the patients who had surgical resection had high-grade dysplasia or cancer. The pre-operative EUS diagnosis was correct in 28.6%. The correct preoperative differentiation between mu-

cinous and non-mucinous lesions was possible in 68.4%. The European Consensus Guidelines' list of risk criteria showed to be a very sensitive (100%) and specific (93.3%) predictor of malignancy. No cystic lesion without an indication for resection showed malignant transformation during the mean observation period of 15.5 months (range 1 - 62).

Conclusion: Pancreatic cystic lesions showed a very low rate of progression or malignant transformation during the first 5 years of observation. EUS alone shows a moderate accuracy to differentiate between serous and mucinous cystic neoplasia. Our results support surveillance for patients who are fit for surgery following the European Consensus Guidelines.

Disclosure: Nothing to disclose

P1082

EFFICACY AND SAFETY OF ENDOSCOPIC TREATMENT OF PERIPANCREATIC COLLECTIONS

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Introduction: Peripancreatic collections (PPC) are complications of acute and chronic pancreatitis (pseudocysts - PC, walled-off necrosis - WON), for which a multimodal approach is recommended, which includes endoscopic therapy.

Aims & Methods: We present real-life data on endoscopic treatment of PPC in a Portuguese center.

Retrospective study of patients submitted to endoscopic treatment of PPC in a Gastroenterology Department between January/2012 and December/2019. Demographic characteristics, type of procedure success and complications were evaluated.

Results: 24 patients were included (PC: n=12; WON: n=12).

PC: The most common indication for drainage was sepsis (n = 5). The mean initial size of the PC was 13.9 cm (7-30). The most used technique was transgastric cystostomy (n=11), either alone (n=1), with placement of plastic pig-tail stents (n=9) or a lumen-apposing metal stent (LAMS) (HotAXIOS™) (n=1); the other patient underwent transpapillary drainage by Endoscopic Retrograde Cholangiopancreatography (n=1). Mean follow-up was 21.9 months (2-60). 1 patient lost follow-up. Technical success was 100% and clinical success was 72.7% (3/11 patients required surgical approach due to failure of endoscopic therapy). There were no Peri-procedure fatalities and post-procedure mortality was 18.2% (n=2), unrelated to the procedure.

WON: The most common indication for drainage was sepsis (n = 8). The average initial size of the WON was 11.2 cm (5-21). Necrosectomy was performed in 11 patients. All patients were submitted to transgastric cystostomy and placement of a LAMS (HotAXIOS™ in 11 and NAGI™ stent in 1). Mean follow-up was 15.7 months (0-36). Technical success was 100% and clinical success 91.7% (11/12). In 5 patients Disconnected Duct Syndrome was present and treated endoscopically, with 100% technical and clinical success. Peri-procedure mortality rate was 8.3% (in the context of septic shock) and post-procedure was 0%.

Conclusion: PPC management should favor a minimally invasive approach. In this cohort, endoscopic treatment was safe and effective on short and long-term follow-up.

Disclosure: Nothing to disclose

P1083

CURRENT APPLICATION OF THE EUROPEAN EVIDENCE-BASED GUIDELINES ON PANCREATIC CYSTIC NEOPLASMS: PRELIMINARY RESULTS FROM A SURVEY PART OF AN UEG DISSEMINATION OF EXISTING CLINICAL PRACTICE GUIDELINES AND STANDARDS PROJECT

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Introduction: Most of available guidelines for the management of pancreatic cystic neoplasms (PCNs) have been developed starting from a low level of evidence, except for European evidence-based guidelines. The aim of this project is to assess their dissemination in Europe with particular attention to low human development index countries where the absence of experienced centers may produce disparities in the treatment offered.

Aims & Methods: An online survey was sponsored through UEG official channels and linked to a new application for smartphones specifically designed for guidelines dissemination. To catch the real-life scenario of guidelines application in Europe, no restrictions were imposed in terms of specialty or center caseload.

Results: Response rate was 52.4% (225/429). Surgery (59.5%) and gastroenterology (36.4%) were the most represented specialties. Participants coming from academic/teaching hospitals were 84.8% and 50% were from centers with a high caseload for PCN. About 77% were aware about European guidelines and 37.3% stated to follow them in the clinical practice. Case vignettes were then used to verify the actual application of European guidelines among their followers revealing that only 10.5% would follow their suggestions in case of main duct dilatation (5-9.9mm), 43.5% in case of an IPMN > 40mm and 74.1% in case of small multifocal branch duct IPMNs.

Regarding low-evidence areas, 17.7% stated that there is enough evidence to suggest surgery in case of main duct dilatation (5-9.9mm) and 38% on the basis of cyst size. In absence of indication for surgery, most of participants would never recommend lifetime discontinuation (78.3%), but only 41.7% believe that there is enough evidence to recommend a lifetime surveillance.

Conclusion: European guidelines dissemination is still partial and requires implementation programs in all European countries. Only one out of three specialists prefer them, but the actual application in the clinical practice is even lower especially when dealing with recommendations that come from low-evidence areas.

Disclosure: Nothing to disclose

P1084

PANCREATIC INTRA-CYSTIC CA 19.9 DOSAGE IN THE MANAGEMENT OF PANCREATIC CYST: USEFUL OR CONFOUNDING? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Pancreatic cystic neoplasms (PCN) are a heterogeneous group of lesions. No accurate markers are available to help in their differentiation. CA 19.9 cyst fluid dosage has been speculated as useful for differential diagnosis of PCN but available data are controversial.

Aims & Methods: The primary outcome measures were the difference of intra-cystic CA 19.9 mean value between mucinous and non-mucinous cyst and its sensitivity and specificity in differentiating these cysts.

The secondary outcome measures were intra-cystic CA 19.9 sensitivity and specificity for the detection of high-grade dysplasia and invasive cancer (termed "malignancy").

We conducted a search for original studies on Pubmed database until January 2020. Specific search terms were "(carbohydrate antigen 19.9 OR CA 19.9) AND pancreatic cystic fluid".

The mean value of intra-cystic CA 19.9 was combined for all the studies. Continues variables were analysed by Student-t test. The sensitivity and specificity of intra-cystic CA 19.9 was combined for all the studies to give pooled value. Pooled estimates were obtained using a random effects model with the generic inverse variance method. The quantity of heterogeneity was assessed by means of the I^2 value. An I^2 value of 25% or lower was considered as trivial heterogeneity, while an I^2 value of 75% or higher as important heterogeneity. A p-value < 0.05 was accepted as statistically significant.

Results: Sixteen cohort studies were enrolled, published from 1986 to 2017. The overall weighted mean value of Ca19.9 in mucinous cysts was 58657,71 U/ml, while, the overall mean value in non-mucinous cysts was 6373,9 U/ml. The difference was not statistically significant (p=0.71). The pooled sensitivity and specificity of CA 19.9 in differentiating mucinous from non-mucinous cysts was respectively 64% (95% CI 49-77%; I^2 93%) and 74% (95% CI 62-83%; I^2 90%). The pooled sensitivity and specificity of CA 19.9 in detecting malignancy was respectively 82% (95% CI 70-90%; I^2 34%) and 66% (95% CI 32-89%; I^2 88%).

Conclusion: The current data don't support the use of intra-cystic CA 19.9 dosage for the differential diagnosis of mucinous and non-mucinous pancreatic cysts but suggest that it could be useful in detecting malignant cysts. However, further studies with bigger and homogeneous sample size and a standardised cut-off value are necessary to confirm it.

Disclosure: Nothing to disclose

P1085

ALREADY EXISTING PSEUDOCYSTS IN ACUTE PANCREATITIS CAN BE AN EARLY MARKER OF CHRONIC PANCREATITIS - ANALYSIS OF 1270 CASES FROM A PROSPECTIVE COHORT

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Introduction: Pseudocysts are the most common late local complications of acute pancreatitis occurring at least four weeks after the onset of the disease.

Aims & Methods: We aimed to analyze the risk factors and outcomes of already existing pseudocysts in acute pancreatitis (AP).

Data were extracted from the Acute Pancreatitis Registry of the Hungarian Pancreatic Study Group. Cases were divided into two groups: patients with already existing pseudocysts (confirmed on imaging within five days from admission) and no pseudocyst. Data on the role of demographic and risk factors and on-admission pancreatic enzymes were analyzed. Case numbers, percentages, and medians with standard deviation were calculated.

Results: Out of the 1270 cases, there were 58 already existing pseudocysts (OLD-P), and 1161 without pseudocyst (NO-P). Alcohol was the most common etiology in OLD-P 18/58 (31.04%). Patients with OLD-P were predominantly male 44/58 (75.86%). In comparison with NO-P, OLD-P cases were associated with: a higher rate of current smoking (28% vs. 41%), a lower body mass index (27.7±5.6 vs. 26.1±7.6 kg/m²), a higher number of previous episodes of acute pancreatitis (1.9±1.9 vs. 2.2±1.4), a higher rate of preexisting chronic pancreatitis (4% vs. 18%) and lower on-admission pancreatic enzyme levels (amylase: 1151±1334 vs. 843±1050 IU/ml; lipase: 2984±5159 vs. 2403±1696 IU/ml).

Conclusion: Preexisting pseudocysts in acute pancreatitis are associated with the risk factors of recurrent and chronic pancreatitis. Therefore, patients presenting with acute pancreatitis and a preexisting pseudocyst need close follow-up as they are at high risk of developing chronic pancreatitis.

Disclosure: Nothing to disclose

P1086 WITHDRAWN

P1087

LOSS OF MTORC1 ACTIVITY COMPROMISE PANCREATIC DUCTAL ADENOCARCINOMA PROGRESSION

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is commonly driven by oncogenic Kras mutations. Mammalian target of rapamycin complex 1 (mTORC1) constitutes an essential downstream target of oncogenic Kras, that is hyperactivated in the majority of PDAC. Here, we investigated the role of mTORC1 in pancreatic carcinogenesis.

Aims & Methods: A well-established mouse model of inflammation-accelerated Kras^{G12D} and loss of p53-driven PDAC was used (KPC). Rptor was conditionally ablated to deactivate the function of mTORC1 *in vivo*. All mice were injected with caerulein for two days to induce acute pancreatitis.

Results: Compared to KPC mice, the pancreas-specific Rptor ablation did not adequately restrain PDAC formation; however, it significantly prolonged the survival of KPC mice. The histological analysis uncovered a less differentiated tumour status with less fibrotic stroma but increased T cells infiltration in PDAC deficient for mTORC1 activity.

Conclusion: These data demonstrate a pro-tumour function of mTORC1 in PDAC by promoting fibrotic reaction and by modulating tumour immunity.

Disclosure: Nothing to disclose

P1088

FEASIBILITY AND OPTIMIZATION OF RNA EXTRACTION FROM EUS-ACQUIRED TISSUE IN PANCREATIC CANCER

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the 2nd leading cause of cancer-related mortality, with transcriptome subtypes related to different prognosis and chemotherapy response.

Nevertheless, RNA extraction from pancreatic tissue is cumbersome for the abundance of RNase and has been performed mainly on surgical samples, representative of < 20% of cases. On the contrary, the majority of PDAC patients undergo Endoscopic UltraSound (EUS)-guided tissue acquisition (EUS-TA), but RNA has been rarely extracted from EUS-TA with scanty results.

Aims & Methods: The aim of our study was to determine the best conditions in terms of needle type and conservation method for RNA extraction from EUS-TA of patients with PDAC.

PDAC cases underwent diagnostic EUS-TA, with collection of samples for RNA extraction. Needles used were 25G Slimline (Boston Scientific) in all patients and then either 20G ProCore (Cook Medical) or 25G Acquire (Boston Scientific); the conservation methods were either snap frozen, RNAlater or Trizol. RNA concentration and quality (RNA Integrity Index; RIN) were analyzed and compared.

Results: A total of 74 samples from 37 PDAC patients were collected and underwent RNA extraction and analysis.

Median RNA concentration was significantly higher in Trizol samples (10,330 pg/ul) compared to snap frozen (637 pg/ul; $p < 0.0001$) or RNALater (190.5 pg/ul; $p < 0.0001$) samples. RIN was similar between Trizol samples (5.15) and snap frozen samples (5.85; $p = 0.8$), while both conservation methods had a borderline significantly higher RIN compared to RNALater samples (2.7; $p = 0.07$ for snap frozen and $p = 0.08$ for Trizol). Among used needles, no significant difference was seen in terms of concentration and RIN among snap frozen and Trizol samples, while ProCore 20G was significantly better for RNALater samples both in terms of median concentration (1,501 pg/ul) and RIN (3.5).

A subset of 6 samples were used to perform q-RT-PCR for a panel of PDAC RNAs with technical success of 100% supporting the clinical usefulness of obtained material.

Conclusion: This is the first study investigating specifically the best methodology for RNA extraction from EUT-TA with results suggesting that a great amount of good quality RNA is obtainable from EUS-TA samples in Trizol. A 20G FNB needle seems superior to smaller needles especially when RNALater is required. The analysis will be extended to ascertain also the composition and cellularity through q-RT-PCR or single-cell RNAseq.

Disclosure: Nothing to disclose

P1089

ROLE OF THE OBESTATIN/GPR39 SYSTEM ON PANCREATIC TUMOR CELL MIGRATION AND INVASION

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Introduction: Obestatin, a 23-amino acid peptide derived from the preproghrelin, was isolated from the stomach in 2005 and was characterized by its binding to the GPR39 receptor. Our group has described the expression of the obestatin/GPR39 system in human pancreatic tumor cell lines, and that, in addition, exogenous obestatin treatment increases the proliferation of these cell lines via the GPR39 receptor. The differences observed in the proliferative capacities of these cells might be due to differences in the expression of key molecules in the obestatin signaling pathway, such as the GPR39 receptor itself or the EGF receptor, to which GPR39 transactivates after obestatin binding.

Aims & Methods: The aim of the present study was to evaluate the effect of obestatin on the migration and the invasion processes in pancreatic tumor cell lines.

Cell lines: PANC-1, RWP-1, and BxPC3.

The invasion assays were carried out using a Transwell chamber. After 16 h at 37 °C, the invasive cells, which had migrated through the membrane, were stained and counted in 10 random high-powered fields per filter by Zeiss Axio Vert.A1 fluorescence microscope. The invasion was calculated using the ImageJ64 analysis software.

Migration was measured by means of a wound healing assay. PANC-1 were wounded with a sterile pipette tip to remove cells by linear scratches. RWP-1 and BxPC-3 cells were analysed in a wound healing assay using IBIDI culture inserts. The progress of migration was photographed immediately after injury and until indicated time after wounding, near the crossing point. The wound was calculated by tracing along the border of the scratch using the ImageJ64 analysis software and using the following equation:

% wound closure = $[(\text{wound area (0h)} - \text{wound area (xh)}) / \text{wound area (0h)}] \times 100$

Results: The evaluation of the cell migration after treatment with obestatin (200 nM; 24h), using 10% FBS as a positive control, produced the results reflected in Table 1.

Obestatin did not modify migration or invasion in any of the cell lines studied. Surprisingly, the co-treatment of obestatin and FBS produced a strong reduction in PANC-1 and BxPC3 migration and invasion capabilities. This effect was not observed in the RWP-1 line, probably due to differences in the mutations present in these cell lines, as well as to the fact that RWP-1 is composed by two subpopulations coexisting in culture.

Migration, 24h	Control	Ob (p)	FBS (p)	FBS+Ob (p, p')
PANC-1	9,68±3,30	7,51±2,55 (0,298)	43,46±8,36 (0,012)	22,23±4,90 (0,044, 0,044)
RWP-1	4,00±0,23	6,38±2,10 (0,189)	56,09±1,09 (0,000)	56,09±1,71 (0,000, 0,499)
BxPC3	13,11±5,31	7,92±4,67 (0,252)	95,13±3,17 (0,000)	68,54±5,26 (0,001, 0,009)
Invasion, 16h	Control	Ob	FBS	FBS+Ob
PANC-1	5,03±0,65	4,78±0,65 (0,543)	16,45±2,05 (0,000)	7,80±0,94 (0,004, 0,002)
BxPC3	3,43±0,40	2,08±0,28 (0,114)	17,08±0,25 (0,000)	8,42±0,49 (0,000, 0,057)

[Table 1. Migration and invasion studies. p is calculated by comparing any treatment with the control and p' with FBS alone]

Conclusion: The results obtained in the pancreatic cancer cell lines of the study show that the obestatin/GPR39 system modulates the migration and invasion of PANC-1 and BxPC3 cells. These data, together with the proliferative capacity observed in these cells, might involve the obestatin/GPR39 system in processes of metastatic cell setting.

Disclosure: Nothing to disclose

P1090

RINT1 DOWNREGULATION DISRUPTS PANCREATIC DUCTAL ADENOCARCINOMA HOMEOSTASIS

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Introduction: Despite intensive basic and translational research, pancreatic ductal adenocarcinoma (PDAC) has still a dismal prognosis. Therefore, understanding cellular homeostasis more in detail and identifying potential druggable targets is crucial to improve patient outcome. RINT1 (RAD50-interacting protein 1) facilitates cell cycle progression, genomic stability, telomere maintenance, and ER-Golgi trafficking. Rare RINT1 missense mutation and RINT1 overexpression were shown to predispose to tumor development including colorectal cancer and Lynch-syndrome type cancers.

Aims & Methods: Therefore, we aimed to investigate the role of RINT1 in human PDAC by database analysis, relevance of RINT1 expression on patient survival suffering from PDAC and shRNA mediated knockdown of RINT1 in human PDAC cell lines.

Results: Of all investigated human PDAC patients, database analysis revealed a copy number alteration in 37% and a mutation frequency of RINT1 in 1.75%, respectively. Additionally, we revealed that protein expression level of RINT1 directly correlated with survival of patients suffering from PDAC. Strong RINT1 expression (score 5) was associated with shortest survival, whereas patients with low levels (score 1) had the best survival. Interestingly, tumor negative for RINT1 expression (score 0) showed a significant increase in poorly differentiated tumors (Grade ≥ 3) compared to RINT1 positive tumors. To characterize cellular function of RINT1, we found that shRNA-mediated RINT1 depletion in human PDAC cell lines led to severe growth defects *in vitro* associated with G2 cell cycle arrest caused by increased DNA-Damage.

In addition, we demonstrated that RINT1 knockdown disrupted Golgi-ER-homeostasis. The overall cellular defects triggered the activation of cell death by apoptosis and partly necroptosis. In subcutaneous and orthotopic xenografts, RINT1 deletion clearly controlled tumor progression. We identified strong immune cell infiltration in athymic nude mice in RINT1-deficient tumors. However, these immune cells do not directly control tumor progression, nevertheless suggesting a potential re-activation of the host immune response *in vivo*.

Conclusion: Our data clearly point out that RINT1 is essential for PDAC survival and represents therefore a putative therapeutic target.

Disclosure: Nothing to disclose

P1091

HEREDITY OF FAMILIAL PANCREATIC CANCER IN A DANISH NATIONAL FAMILY COHORT

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Introduction: Familial Pancreatic Cancer (FPC) is responsible for up to 10% of all cases of pancreatic ductal adenocarcinoma (PDAC). Individuals predisposed for FPC have an estimated lifetime risk of 18-38% of developing PDAC (1, 2). The heredity of FPC is sparsely investigated. While heredity of PDAC has been estimated to be 36% in an European population-based twin study (3), the genetic contribution to FPC in the Danish population has not been assessed.

Aims & Methods: A national cohort of 27 Danish families with disposition for FPC are currently included in a screening program for PDAC at the Department of Medical Gastroenterology, Odense University Hospital. Familial disposition for FPC is defined by presence of either:

- A) at least 2 PDAC cases among first degree relatives (FDR) with at least one of the cases debuting < 50 years of age, or;
- B) at least 3 PDAC cases among FDRs (4).

Family members included in the screening program were interviewed and the following data were obtained: Cases of PDAC among FDRs (e.g., familial relation, age at diagnosis of PDAC), number of affected/unaffected siblings, and baseline characteristics including smoking and alcohol status.

Heredity estimates for FPC in the predisposed families were calculated using a generalized mixed effect model, with calculation of an intra class correlation coefficient (ICC).

Results: Among 27 Danish families with predisposition for FPC, 81 cases of PDAC were identified. The median age at diagnosis of PDAC was 64 years, and median time from diagnosis to death was 7.5 months. As of September 1st 2018, 64 FDRs of the PDAC patients were included in the screening program. Among the included FDRs the median age was 60 years, and the median length of inclusion in the screening program was 84 months. Pedigrees for the screened FDRs included a total of 174 individuals in sibship, with sibship sizes ranging from 2-11. We estimated an ICC of 0.17 (95% CI: 0-0.43), corresponding to a heredity of 34% in the FPC family cohort.

Conclusion: The estimated heredity of FPC in a Danish family cohort serves as a solid basis for conducting molecular genetics and omics analysis of the cohort which are currently underway.

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Disclosure: Nothing to disclose

P1092

KRAS ACTIVATION IN THE CONTEXT OF BRCA2 DEFICIENCY DRIVES DEDIFFERENTIATION OF DUCTAL ORGANIDS DERIVED FROM HUMAN PLURIPOTENT STEM CELLS

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) still has a dismal prognosis and is predicted to be the second most leading cause of cancer-related death in 2030. Up to 10% of PDACs occur in families with at least two affected first-degree relatives. In approx. 20% of these familial pancreatic cancer (FPC) cases, inheritance has been attributed to a set of mutations in genes most of which are involved in DNA damage repair like *BRCA1/2*, *ATM*, and *PALPB2*.

Aims & Methods: We aimed to establish a human pluripotent stem cell-based model system to investigate how defective *BRCA2* associated with known cancer driving mutations impact on duct-like cells. Using CRISPR/Cas9 genome editing, we created a large deletion in the *BRCA2* locus in human embryonic stem cells (hESCs) mimicking germline inactivation of *BRCA2* in FPC patients. Moreover, we introduced an inducible *KRAS*^{G12D} expression cassette into these cells via a *piggyBac* transposon system followed by applying these cells onto our pancreatic duct-like organoid (PDLO) differentiation platform.

Results: hESCs with a heterozygous knockout of *BRCA2* (*BRCA2*-het) efficiently differentiated towards the pancreatic lineage and formed ring-like ductal organoids. Activation of *KRAS*^{G12D} in *BRCA2*-het PDLOs caused an upregulation of epithelial-to-mesenchymal transition (EMT) markers and induced a pro-apoptotic and pro-senescence program. These changes

in expression profile and growth phenotype were stronger compared to oncogenic KRAS effects detected in *BRCA2*-wt (wildtype) organoids. In long-term stimulation experiments, we observed widespread cell dissemination of *BRCA2*-het PDLOs resembling a “dedifferentiation” phenotype, the latter being absent in WT PDLOs induced with *KRAS*^{G12D}. Orthotopic transplantation of *KRAS*-induced *BRCA2*-mutant PDLOs further helped to characterize this phenotype.

Conclusion: In sum, by combining mutations in a common cancer susceptibility gene in hESCs with *KRAS* activation in long-term PDLO cultures, we were able to evoke features of dysplastic growth and neoplasia formation *in vitro*. Thus, we present a powerful tool to model FPC and provide insights into the early molecular and functional consequences of a given oncogenic mutation in a human duct. This also opens unique opportunities for future applications such as drug screenings in a specific genetic background.

Disclosure: Nothing to disclose

P1093

PRECLINICAL VALIDATION OF NOVEL GENOTYPE-SPECIFIC THERAPEUTIC CONCEPTS FOR *ATM*-DEFICIENT PANCREATIC CANCER

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Introduction: The prognosis of pancreatic ductal adenocarcinoma (PDAC) is still dismal despite decades of research leading to an improved understanding of its mutational landscape. The phase III POLO trial recently introduced the first effective targeted therapy in PDAC by implementing the PARP inhibitor (PARPi) olaparib as a treatment option for maintenance therapy following treatment with FOLFIRINOX in germline *BRCA1/2* mutated patients. However, *BRCA1/2* mutations comprise only a small proportion of genes involved in DNA damage response (DDR) within the genomic unstable PDAC subtype, whereas the serine/threonine protein kinase Ataxia-telangiectasia-mutated (ATM) is the most frequently mutated DDR gene that occurs in sporadic and familial PDAC. Our lab has previously demonstrated that deletion of ATM in a mouse model of pancreatic cancer accelerates tumorigenesis, metastasis and leads to genomic instable tumors that are vulnerable to simultaneous inhibition of PARP, ATR and DNA-PKc.

Aims & Methods: Up to our current knowledge the most effective conventional chemotherapy for DDR-defective cancer is platinum-based. The most potent platinum derivate as well as PARPi in terms of cytotoxicity have not yet been conclusively determined.

Based on the *Atm*^{fl/fl}; *LSL-Kras*^{G12D/+}; *Ptf1a*^{Cre/+} (AKC) and *LSL-Kras*^{G12D/+}; *Ptf1a*^{Cre/+} (KC) mouse model primary AKC and KC PDAC cell lines were established. We performed a systematic drug screen on several *ATM*-deficient (AKC) and *ATM*-proficient (KC) primary PDAC cells:

- (i) to assess genotype-specific vulnerabilities,
- (ii) to identify the most effective platinum derivate and PARPi for subsequent synergistic interactions and;
- (iii) to lower toxicity and increase efficiency upon drug combination.

Results: Interestingly, contrasting with *BRCA1/2*-mutant PDAC, *ATM* mutations do not entail higher sensitivity toward platinum-based chemotherapy. Intriguingly, among conventional chemotherapeutics the topoisomerase inhibitors (TOPI) irinotecan and etoposide act genotype-specific and seem to be more efficient in terms of cell death than platinum derivatives. This is in line with previous findings of selective hypersensitivity due to blockage of replication-dependent strand cleavage upon TOP inhibition.

Our findings are supplemented by *ATM*-deficient and *ATM*-proficient pancreatic organoids and most efficient synergistic interactions will be validated *in vivo*.

Conclusion: Thus, we provide novel genotype-specific therapeutic concepts to pave the way for clinical trials in *ATM*-deficient PDAC based on preclinical determination of the most effective PARPi and PARPi-based combinational therapy.

Disclosure: Nothing to disclose

P1094

EZH2, AN EPIGENETIC FACTOR INVOLVED IN ONCOGENIC PROPERTIES OF *ATM* DEFICIENT PDAC SUBTYPES?

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Introduction: Despite decades of extensive basic and translational research improving our understanding of pancreatic ductal adenocarcinoma (PDAC) biology, PDAC is predicted to become the second-leading cause of cancer-related death in 2030. Due to its resistance towards conventional therapies and its heterogeneous mutational landscape, the molecular stratification and the development of targeted therapeutic options is essential for improving survival in PDAC patients. PDAC harbours recurrent functional mutations of the DNA damage response serine/threonine kinase ATM (ataxia telangiectasia mutated), which has been shown to accelerate tumorigenesis as well as tumour cell plasticity.

We previously found that loss of ATM coincides with oncogenic programs including epithelial-mesenchymal transition (EMT) and stemness behaviour. Preliminary data show an overexpression of the histone-methyltransferase EZH2 (enhancer of zeste homolog 2) in our AKC (*Ptf1a*^{Cre/+}; *Atm*^{fl/fl}; *LSL-Kras*^{G12D/+}) transgenic mouse model, which leads us to question the role of this epigenetic factor in *ATM*-deficient PDAC subtypes.

Aims & Methods: In order to decipher oncogenic EZH2-functions during pancreatic tumorigenesis, a transgenic mouse model displaying both *ATM* and *EZH2* depletion in a *Kras*^{G12D} activated context was generated (AKEC mice). Mice were evaluated for phenotypic differences, survival comparison, and histopathological analyses were performed to define the role of EZH2 during PDAC development. Additionally, tumor cells were isolated from AKC and AKEC mice, as well as CRISPR/Cas9 strategy was used, to decipher the molecular and functional involvements related to ATM and EZH2 depletion.

Results: Initial data from the characterization of our model suggest that AKEC mice experience longer survival and a reduced tumour incidence compared to AKC animals. Interestingly, *in vitro* analyses conducted with isolated pancreatic tumour cells reveal that EZH2-loss is associated with the regulation of several EMT genes, suggesting a favourable role of this epigenetic factor in invasive properties of *ATM*-deficient PDAC cells. Furthermore, we observe that loss of ATM is associated with modifications of the post-translational regulation of the protein EZH2, which could explain its overexpression and its damaging activity during pancreatic tumorigenesis.

Conclusion: Altogether, our results suggest that *ATM*-deficiency significantly impacts EZH2-dependant gene regulation and functions, hence molecular stratification of ATM status prior to pharmacologically interfering with EZH2 inhibitors in PDAC therapies is considered essential.

Disclosure: Nothing to disclose

P1095

MAINTENANCE THERAPY FOR ATM-DEFICIENT PANCREATIC CANCER BY MULTIPLE DNA REPAIR PATHWAY INHIBITION AFTER PLATINUM-BASED CHEMOTHERAPY

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Introduction: Mutations in DNA-damage repair (DDR) genes can ascribe vulnerability toward PARP1 inhibitors allowing tailored interventions in certain cancer types. Personalized medicine in treating pancreatic ductal adenocarcinoma (PDAC) is still in its infancies albeit PDAC-related death is projected rising over the next decade. Most recently, PARP1-inhibitor maintenance therapy after platinum-based induction improved progression-free survival in germline BRCA1/2 mutated PDAC. Transferability of such concept to other mutant DDR genes is unclear.

Aims & Methods: We conducted a placebo-controlled, three-armed pre-clinical trial to evaluate the efficacy of multi-DDR interference (mDDRi) as a maintenance therapy vs. FOLFIRINOX-ongoing implemented with ATM-deficient PDAC lines upon orthotopic transplantation. Kaplan-Meier analysis, time resolved cross-sectional imaging by MRI, histology as well as *in vitro* analysis was applied as analytical readout.

Results: Median overall survival was significantly longer in the maintenance arm followed by FOLFIRINOX-ongoing and placebo. Survival benefit in the maintenance arm was mirrored in highest DNA damage load, accompanied by reduced primary cancer size and metastatic load. *In vitro* analysis suggests FOLFIRINOX-driven selection of more invasive sub-clones, erased by the subsequent mDDRi treatment, in line with reduced metastatic burden *in vivo*.

Conclusion: Collectively, this preclinical trial substantiates mDDRi as novel therapeutic option in PDAC and extends the concept to non-BRCA1/2 mutant PDAC.

Disclosure: Nothing to disclose

P1096

LOW-FREQUENCY OF RABL3 PATHOGENETIC VARIANTS IN HEREDITARY AND FAMILIAL PANCREATIC CANCER

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Introduction: Pancreatic duct adenocarcinoma (PDAC) risk can be inherited as hereditary and familial pancreatic cancer (HPC and FPC). HPC is a genetically confirmed PDAC predisposition with an autosomal dominant transmission of inheritance. FPC is clinically diagnosed when three relatives have PDAC, or when two relatives are affected, with one first degree relative. Approximately 5-10% of all PDACs fit these criteria. Nissim et

al.[1] recently reported a four-generation pedigree with a history of five relatives with PDAC and multiple other occurrences of cancer (melanoma, breast, central nervous system, colon, stomach, liver, and an unknown primary cancers) spanning multiple generations. Of the 15 individuals with cancer, 6 had synchronous tumor primary.

In 2 of 5 family members a heterozygous ser36-to-ter pathogenetic variant (PV) in the member of the RAS oncogene family-like 3 (RABL3) gene was described. In another family with cancer predisposition, authors identified heterozygosity for an arg184-to-gln (R184Q) PV in RABL3 in 3 sibs, 2 with PDACs and 1 with colon cancer. The truncated RABL3 protein accelerates KRAS prenylation and requires RAS proteins to promote cell proliferation. Expression of mutant RABL3 in HEK293T cells resulted in enhanced cell proliferation and Zebrafish with truncated RABL3 protein developed cancers at a statistically significant elevated rate compared to wildtype sibs.

Aims & Methods: Aim of our study was to confirm in an Italian population of 30 FPCs, 28 HPCs, 8 sporadic PCs with one first degree affected by PC and 61 normal controls (NC) with negative family history for cancers, the presence of the two pathogenetic variants of RABL3 gene.

We analyzed: 30 FPCs (18 females, 12 males, mean age 55,50±13,99), of whom 4 families and 18 not kindred, 28 HPCs (15 females, 13 males, mean age 54,14±12,83) of whom 6 families and 15 not kindred, 8 sporadic PCs with one first degree affected by PC and 61 NC age-matched, with negative family history for cancers in their three generations pedigree and PREMM5 predictive software< 2.5%. gDNA was extracted starting from 200uL of whole blood previously frozen in EDTA.

Library for high throughput sequencing was prepared starting from amplicons for the coding region, for human RABL3 protein, which circumvent p.Ser36 (position chr3:120,730,727 hg38). The PCR amplification was performed using the following primers:

hRABL3-S36Forw-2*:

TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGtttcagccttctcttatgtga

hRABL3-S36Rev-2*:

GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGaagacacatactctgacatccac

hRABL3-Arg184Forw3*:

TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGcaacgagcttggttctcta

hRABL3-Arg184Rev-3*:

GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGaataaaggctcataggattctacaaaaa

Sequencing was performed on MiSeq (Illumina) in PE(pair end) , generating approx. 20k reads for each sample, 150nt long. After demultiplex, reads are aligned with bwa (Burrows-Wheeler Aligner) on hg38 version. Variant calling was performed using Freebayes with default parameters.

Results: Of the 30 FPCs, 28 HPCs, 8 sporadic PCs with one FDR affected by PC and 61 normal controls with negative family history for cancers no one presented the two RABL3 PVs associated with HPC.

Conclusion: RABL3 PVs might be of low-frequency concentrated in limited geographical areas. They may, however, play a substantial role in disease susceptibility.

References: Nissim et al. "Mutations in RABL3 alter KRAS prenylation and are associated with hereditary pancreatic cancer." Nat Genet. 2019;51:1308-1314.

Disclosure: Nothing to disclose

P1097

PROGNOSTIC VALUE OF AGRIN EXPRESSION IN PATIENTS WITH PANCREATIC CANCER

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Introduction: Molecular prognostic markers are needed in patients with pancreatic adenocarcinoma (PADC). Agrin (AGRN) is a protein released by tumor cells that promotes metastasis and is overexpressed in early stages of tumor progression. Exosomes are extracellular vesicles released by cells that mediate inter-cellular communication. In the context of cancer, they promote tumor progression by modulating cells in the tumor microenvironment. Identification of tumor markers in exosomes is an attractive strategy to improve prognostic stratification of PADC patients, since these vesicles are present in all body fluids.

Aims & Methods: Our goal was to evaluate the value of AGRN expression by the primary tumor and in circulating exosomes to predict the prognosis of PADC patients during follow-up (FU). We conducted a prospective single-center cohort study including patients diagnosed with PADC treated at Hospital Beatriz Ângelo (Portugal) between October 2017 and October 2019. Tumor samples were collected during surgery or endoscopic ultrasound-guided puncture and blood samples were collected before these procedures. After processing, the samples were cryopreserved at -80°C for later analysis. In each tumor sample, the expression of AGRN was quantified by immunohistochemistry and presented as a score from 0-12 described elsewhere. The percentage of circulating exosomes positive for AGRN expression was quantified by flow cytometry. We collected data about disease progression (detected at computed tomography or by elevation of CA 19.9) and death.

Results: Thirty-five patients were included, 20 (57%) of whom were men with mean age of 70±8 years. The TNM stage at diagnosis was I in 6 (17%) patients, II in 10 (29%) patients, III in 6 (17%) patients and IV in 13 (37%) patients. About half of patients (54%, n=19) presented with resectable disease and 3 (9%) with borderline resectable disease at diagnosis; overall, 20 (57%) patients underwent surgery. About one-third of patients (34%, n=12) presented with metastatic disease and 1 (3%) with locally advanced disease. Median FU time was 10 months (mos).

Median AGRN score was 5 (mean 5±3, IQR 0-12) and median percentage of positive exosomes was 8% (mean 16±23, IQR 3-91); both parameters were higher in patients with more advanced disease at TNM stage III/IV (6 vs. 4, p=0.97 and 8 vs. 6, p=0.14, respectively). During FU, 14 (40%) patients had disease progression and 19 (54%) died.

Median AGRN score was higher in patients who had disease progression (6 vs 4, p=0.63) or death (6 vs 4, p=0.55) during FU. In a survival analysis, the time for disease progression (plogrank=0.63) or death (plogrank = 0.29) was shorter in patients with a higher AGRN score (10 vs. 14 mos and 12 vs. 21 mos, respectively).

Median percentage of positive exosomes was also higher in patients who had disease progression (8 vs 6, p=0.62) or death (10 vs 7, p=0.62). The time for disease progression (plogrank = 0.43) or death (plogrank=0.07) was also shorter in patients with a higher proportion of positive exosomes (7 vs. 15 mos and 11 vs. 19 mos, respectively).

Conclusion: In our cohort, most patients presented at a relatively early disease stage and were able to undergo surgery resection. AGRN expression in tumor samples did not appear to be associated with higher rate of disease progression or death. However, AGRN expression in circulating exosomes showed a tendency to be associated with shorter survival. The major limitation of our study is the reduced sample size. A study with a larger sample size is needed and we hope it will yield more robust results.

References: Tian C, Öhlund D, Rickelt S et al. Cancer-cell-derived matrix proteins promote metastasis in pancreatic ductal adenocarcinoma. *Cancer Research*. 2020. doi: 10.1158/0008-5472.CAN-19-2578

Disclosure: Nothing to disclose

P1098

A NOVEL SYNERGISTIC THERAPY APPROACH TO TREAT DNA DAMAGE REPAIR DEFICIENT PANCREATIC CANCER

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Introduction: In general, the diagnosis of pancreatic ductal adenocarcinoma (PDAC) is associated with high mortality rates. State of the art therapy approaches consider the mutational make up of different tumors, however in PDAC often failed. One of the most promising PDAC subtypes to specifically target is the genomic unstable one counting for more than 10% of all cases. ATM serine/threonine kinase (ATM) represents the most commonly mutated gene in this subgroup and is eminent for DNA-damage response (DDR) by homologous recombination (HR). Recently, interference with the DDR machinery first succeeded using the PARP inhibitor olaparib in a phase III trial as maintenance therapy in advanced PDAC after platinum-based induction chemotherapy. Here, we aimed on establishing a novel genotype-tailored targeted therapy for DDR-deficient cancer.

Aims & Methods: Primary murine AKC(Atm^{fl/fl}; LSL-Kras^{G12D/+}; Ptf1a^{Cre/+}) and KC (LSL-Kras^{G12D/+}; Ptf1a^{Cre/+}) PDAC cell lines were generated. For human translation either one or both ATM alleles were deleted in MIA PaCa-2 and PANC-1 cell lines using a CRISPR/Cas9 approach. These cell lines undergone a customized screening for combinational synergies upon ATM-deficiency, with further validation in an *in vivo* setting.

Results: The combinational inhibition of PARP, ATR, and DNA-PKcs (PAD) causes synthetic lethality in ATM-deficient murine and human PDAC. As a consequence of PAD therapy aneuploidy and a dramatic increase of mitosis aberrations could be seen. Moreover, PAD induced PARP trapping and replication fork stalling, altogether resulting in P53-mediated apoptosis. *In vivo* confirmation underlined superior AKC genotype specific tumor control with PAD upon transplantation. Most importantly, human translation showed the same synergistic effects of PAD *in vitro* and *in vivo*. Finally, chemical inhibition of ATM sensitized ATM-proficient human PDAC cells to PAD with long-term tumor control *in vivo*. This approach could further be transferred to patient derived pancreatic organoids revealing a significant response to ATM inhibition and PAD therapy.

Conclusion: Here, we present a novel preclinically elaborated therapeutic approach for combinational targeting of ATM-deficient PDAC, that could be also extendedly implemented in a genotype-independent manner by chemical ATM inhibition.

Disclosure: Nothing to disclose

P1099 WITHDRAWN

P1100

ENDOSCOPIC DUODENAL STENT PLACEMENT VERSUS SURGICAL GASTROJEJUNOSTOMY FOR UNRESECTABLE PANCREATIC CANCER PATIENTS WITH DUODENAL STENOSIS BEFORE INTRODUCTION OF FIRST-LINE CHEMOTHERAPY (GASPACHO STUDY)

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Introduction: Endoscopic duodenal stent placement (EDSP) is usually applied as palliative care for patients with poor prognosis within 2 months, while surgical gastrojejunostomy (SGJJ) has been recommended for patients who receive chemotherapy.

However, recent advances in stent devices and techniques have allowed EDSP to be safely performed and expanded the indications even in unresectable pancreatic cancer (UPC) patients with duodenal stenosis who receive chemotherapy. In the context of recent intensive chemotherapies such as FOLFIRINOX and gemcitabine plus nab-paclitaxel, whether EDSP or SGJJ is preferable for UPC patients with duodenal stenosis before che-

motherapy remains controversial. Little information has been reported about treatment outcomes of EDSP or SGJJ in UPC patients with duodenal stenosis who are candidates for intensive chemotherapies.

Aims & Methods: **Aim:** To clarify real-world outcomes of treatments using EDSP or SGJJ for previously untreated UPC patients with duodenal stenosis who received chemotherapy.

Methods: This multi-center retrospective study included 24 hospitals in Japan. Patient selection criteria were: 1) UPC with duodenal stenosis diagnosis from imaging with histology or cytology; 2) aged 20-80 years; 3) gastric outlet obstruction scoring system (GOOSS) score 0 or 1; 4) good performance status; 5) eligible for chemotherapy and receiving EDSP or SGJJ between January 2014 and December 2017; 6) no history of gastrectomy; and 7) no prior intervention for gastric outlet obstruction. Technical success was defined as EDSP and SGJJ performed as planned and on schedule. Clinical success was defined as sustained food intake (GOOSS ≥ 2) within 2 weeks after technical success.

Results: One hundred patients (EDSP, n=57; SGJJ, n=43) met the inclusion criteria. In terms of patient characteristics, the proportion of patients ≥ 75 years old was higher in the EDSP group (33%) than in the SGJJ group (9%), although little difference was seen in other characteristics. Frequency of moderate to severe adverse events was 18% in the EDSP group and 12% in the SGJJ group. In both groups, the technical success rate was 100% and the clinical success rate was 95%. In the 95 patients with clinical success (EDSP, n=54; SGJJ, n=41), median time until resumption of food intake after first EDSP or SGJJ was 3 days (range, 2-8 days) and 5 days (range, 3-25 days), respectively. The success rate of chemotherapy introduction was 63% in each group. Median overall survival from the first day of EDSP or SGJJ was 5.9 months and 6.0 months, respectively. In 63 patients receiving chemotherapy, the median interval between the procedure and chemotherapy introduction was shorter for EDSP (14 days; range, 3-43 days) than for SGJJ (32 days; range, 13-97 days). In 63 patients receiving chemotherapy, the median overall survival from chemotherapy introduction was 8.8 months in the EDSP group and 7.0 months in the SGJJ group. These results were consistent with age-adjusted propensity score-matching.

Conclusion: This study suggested that EDSP achieved comparable outcomes to SGJJ in UPC patients with duodenal stenosis who planned to receive chemotherapy. Chemotherapy was initiated earlier in patients treated with EDSP than those treated with SGJJ.

Disclosure: Nothing to disclose

P1101

PANCREATIC STEATOSIS ON COMPUTED TOMOGRAPHY IS AN EARLY IMAGING FEATURE IN PATIENTS WITH PRE-DIAGNOSTIC PANCREATIC CANCER - A CASE-CONTROL STUDY

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Introduction: The prevalence of pancreatic ductal adenocarcinoma (PDAC) is on the rise, driven by factors such as aging and increasing prevalence of obesity and diabetes mellitus. To improve the poor survival rate of PDAC (9%), early detection that enables curable treatment is vital. Recently, pancreatic steatosis has gained novel interest as a risk factor for pancreatic cancer.

This study aimed to investigate if pancreatic steatosis on Computed Tomography (CT) is an early imaging feature in patients with pre-diagnostic PDAC

Aims & Methods: A retrospective, observational, case-control study was performed. Cases with histopathological confirmed PDAC diagnosed at our hospital between 2010 and 2016 were reviewed for abdominal non-contrast CT-imaging 1 month - 3 years prior to the diagnosis of PDAC. Cases were matched with controls in a rate of 1:4 based on age, gender and date of imaging (+/-3 months). Unenhanced CT-images of cases and controls were evaluated for pancreatic steatosis by an experienced radiologist, who was blinded for case-control status. The pancreas-to-spleen (P/S) attenuation ratio and the presence of pancreatic steatosis, defined as a P/S ratio < 0.70, were calculated and compared between cases and controls.

Results: In total, 32 cases and 117 age- and gender matched controls were included in the study. In cases, CT images were obtained with a median of 7.6 months (range 1.6 - 30.8) before the diagnosis of PDAC. Mean age in years was 68.1 (11.6) for cases and 68.8 (10.3) for controls, mean BMI was 29.6 (4.9) in cases versus 29.2 (5.5) in controls. Pancreatic steatosis was present in 71.9% of cases compared to 45.3% of controls (OR 3.09 (1.32-7.24), $p = 0.0094$) (Table 1). The association between pancreatic steatosis and cancer was strongest in the subgroup who underwent imaging within 6 months of diagnosis (OR 5.91 (1.45-24.9), $p = 0.0081$). Adjusted for BMI and diabetes mellitus, pancreatic steatosis on CT remained a significant independent predictor for PDAC (adjusted OR 2.70 (1.14 - 6.58), $p = 0.0369$).

Conclusion: In conclusion, pancreatic steatosis measured on CT is independently associated with PDAC in up to three years before the clinical diagnosis. Patients with pancreatic steatosis had the odds of being diagnosed with PDAC almost three times higher compared to those without pancreatic steatosis. Since screening for PDAC is only recommended in high-risk individuals, this novel imaging feature may be used to identify high-risk individuals for PDAC and to stratify the risk of cancer in individuals that already undergo PDAC screening.

	Cases (n = 32)	Controls (n = 117)	Odds Ratio (95% CI)	p-value
P / S < 0.70	23 (71.9%)	53 (45.3%)	3.09 (1.32 - 7.24)	0.0094
• ≤6 months prior to diagnosis	11 (78.6%)	18 (38.3%)	5.91 (1.45 - 24.9)	0.0081
• >6 months prior to diagnosis	12 (66.7%)	35 (50.0%)	2.00 (0.67 - 5.93)	0.2061
P / S, median (IQR)	0.61 (0.34)	0.73 (0.50)		0.0628
• ≤6 months prior to diagnosis	0.55 (0.29)	0.76 (0.48)		0.0388
• >6 months prior to diagnosis	0.65 (0.40)	0.69 (0.55)		0.4786

P/S; pancreas-to-spleen ratio Pancreatic steatosis on CT is defined as a pancreas-to-spleen ratio of less than 0.70

[Table 1. Measures of pancreatic steatosis on CT in cases versus controls]

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P1102

RISK FACTORS AND INCIDENCE OF PANCREATIC CANCER AFTER DETECTION OF HELICOBACTER PYLORI INFECTION: A LARGE COHORT STUDY

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Introduction: Pancreatic cancer (PaC) remains the fourth leading cause of all cancer related deaths in the USA. Continuous efforts are being established to identify patients with predisposing risk factors for PaC. Limited small case-control studies describe the relationship between the incidence of *H pylori* and PaC.

Aims & Methods: We aim to establish the incidence and risk factors for PaC after detection of *H pylori* using a large cohort of patients in the USA and identify how treatment affects cancer risk. A population-based study was conducted using a cloud-based, HIPAA-enabled web platform called Explorys (IBM, New York) to collect aggregated de-identified electronic health records from 1999-2019. SNOMED criteria was utilized to identify patients with "malignant tumor of pancreas" and "*Helicobacter pylori*" infection including 1) positive stool antigen test, 2) positive serum antibody (first time occurrence) and 3) presence of *H pylori* infection (first time occurrence). A temporal relationship was established to evaluate the incidence of PaC after positive *H pylori* detection. The role of treatment was also established by searching for drug ingredients amoxicillin, clarithromycin, tetracycline, metronidazole (in combination therapy) and pharmacology class of proton-pump inhibitors. The primary outcome was a diagnosis of pancreatic cancer 30 days or more after detection of *H pylori* infection. Secondary outcomes evaluated all-cause mortality, and the role of PaC incidence after *H pylori* treatment. Standardized incidence ratios (SIR) and odds ratios (OR) were calculated and analyzed.

Results: Explorys identified 205,120 patients with *H pylori* infection, of which 850 developed PaC. In comparison, 470 patients were identified with PaC after *H pylori* infection with an established treatment regime. Patients who received treatment for their *H pylori* infection had a decreased risk of PaC vs. those without treatment (SIR 0.4% vs. 0.2%, $P < 0.0001$). Males, elderly patients (>65) and African-Americans were more prone to develop PaC after *H pylori* infection, regardless of treatment. Tobacco use increased risk of PaC regardless of *H pylori* infection. All-cause mortality significantly increased with the presence of PaC, with or without treatment of *H pylori* infection.

	H. pylori (N = 205, 120)	H. pylori with PaC (N = 850)	P-value (no PaC vs. PaC)	H. pylori with therapy to PaC (N = 470)	P-value (PaC vs. PaC + Treatment)	P value (no PaC vs. PaC + Treatment)
Male	79,820	420	<0.0001	230	0.8619	<0.0001
Age						
18-65	128,640	260	<0.0001	160	0.2043	<0.0001
>65	73,600	580	<0.0001	310	0.4143	<0.0001
Race						
Caucasian	122,740	520	0.4061	290	0.8583	0.4014
African American	42,640	230	<0.0001	140	0.2960	<0.0001
Asian	9,250	30	0.1603	20	0.4660	0.8345
Hispanic/Latin American	5,720	10	0.0047	< 10	-	-
Tobacco use	150,740	630	0.6924	410	<0.0001	<0.0001
Deceased	13,390	380	<0.0001	220	0.4633	<0.0001

[Comparison of Patients with *H. pylori* who did and did not Develop Pancreatic Cancer]

Conclusion: In this large-population based study, diagnosis of *H pylori* infection was found to have a significantly higher risk of pancreatic cancer in males, African-Americans, elderly patients, and smokers. Treatment of *H pylori* infection decreased the risk of pancreatic cancer. Longitudinal prospective studies are necessary to further delineate this relationship.

Disclosure: Nothing to disclose

P1103

NANOLIPOSOMAL IRINOTECAN WITH FLUOROURACIL AND FOLINIC ACID IN METASTATIC PANCREATIC CANCER AFTER PREVIOUS GEMCITABINE-BASED THERAPY: A REAL WORLD EXPERIENCE

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Introduction: Nanoliposomal irinotecan (nal-IRI) is an effective and safe therapy, accompanied with 5-fluorouracil (5-FU) and leucovorin (LV), for metastatic pancreatic ductal adenocarcinoma whose disease progressed after gemcitabine-based chemotherapy. In NAPOLI-1 study, this regimen showed survival benefit and was proved by FDA.

Aims & Methods: Our aim was to evaluate the effectiveness and safety of nal-IRI + 5-FU/LV regimen for patients with metastatic pancreatic cancer and gemcitabine-based treatment failure in the real world. We retrospectively collected the data of the patients with metastatic pancreatic adenocarcinoma who had a gemcitabine-based treatment failure and were treated by nal-IRI-based regimen in Taipei Veterans General Hospital, a tertiary medical center in Taiwan.

Results: From August, 2018 to June, 2019, sixty-seven patients who received nal-IRI + 5-FU/LV regimen were identified. The median age: 65 years-old, male sex: 52%. ECOG performance status 0-2. The median initial dose of nal-IRI was 36.8 mg/m² and the dose intensity was 106.5 mg/m² within 6 weeks. The median overall survival was 4.8 months (95% confidence interval (CI): 3.3 - 6.4) and median progression-free survival was 2.4 months (95% CI: 1.3 - 3.6). Six-month OS and PFS rates were 42% and 22%. Objective response and disease control rates were 10.4% and 38.8%. Among the patients, only 41 patients met the inclusion criteria of NAPOLI-1 study (ECOG 0-1, adequate haematological (including absolute neutrophil count >1.5 × 10⁹ cells per L), hepatic (including normal serum total bilirubin and albumin levels ≥30 g/L), and renal function). The median overall survival (6.33 months) became consistent with the NAPOLI-1. The most common all grade adverse effects were anemia (73.9%), nausea (66.2%) and fatigue (61.5%). Most common grades 3-4 adverse effects were neutropenia (21.5%), anemia (18.5%) and diarrhea (15.4%).

Conclusion: In the real-world, nal-IRI + 5-FU/LV is effective and well-tolerated in patients with metastatic pancreatic adenocarcinoma that progressed after gemcitabine-based therapy.

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Disclosure: Nothing to disclose

P1104

PREVALENCE OF MALNUTRITION, CACHEXIA, AND ANOREXIA IN UNRESECTABLE PANCREATIC CANCER PATIENTS

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Introduction: In advanced pancreatic ductal adenocarcinoma (PDAC), malnutrition, cachexia, and anorexia are frequently diagnosed, but data on their prevalence are sparse and heterogeneous and often obtained with limited tools retrospectively.

Aims & Methods: We investigated prospectively the nutritional status of patients within the PAC-MAIN study (PANcreatic Cancer MALnutrition and pancreatic exocrine iNsufficiency, NCT04112836). We analyzed the rates of malnutrition according to Mini-Nutritional Assessment (MNA) score, cachexia and anorexia with 12-item functional assessment of anorexia/cachexia subscale (FAACT), as well as quality of life using EORTC QLQ-PAN26 scale in locally advanced or metastatic PDAC patients with confirmed histological diagnosis who were planned for chemotherapy. Data are shown as median and interquartile range (IQR).

Results: Data on the first 60 enrolled patients are presented: 36 males, median age 64.7 (IQR 53.2 to 71.9). In 39 patients, the tumors were located in the head of the pancreas and in 27, in the body-tail, with the mean size of 47 mm. The median BMI was 24.7 (IQR 22 to 26.3). Eight patients had clinical evidence of steatorrhea, while 26.7% of patients were under pancreatic exocrine enzyme replacement therapy. 26.7% of patients were malnourished, while 67.7% were at risk of malnutrition based on MNA score (median MNA score 9, IQR 7 to 10). The median FAACT score was 19 (IQR 13.25 to 24), with all patients being below the cut-off of normality of 37. The median EORTC QLQ-PAN26 scale value was 54 (IQR 45 to 61.75).

Conclusion: The majority of patients with advanced PDAC are either malnourished or at risk of malnutrition and have reduced quality of life and significant anorexia/cachexia. PAC-MAIN study will prospectively in-

investigate the impact of patient's nutritional status and quality of life on the clinical course of patients with advanced PDAC treated with chemotherapy.

Disclosure: Nothing to disclose

P1105

PANCREATIC EXOCRINE INSUFFICIENCY AND PANCREATIC ENZYME REPLACEMENT THERAPY IN PATIENTS WITH ADVANCED PANCREATIC CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Pancreatic cancer is the 4th leading cause of cancer mortality. Most patients are diagnosed with advanced pancreatic cancer (APC), either at locally advanced or metastatic stages and have a high rate of malnutrition and weight loss which are associated with poor outcomes. Pancreatic exocrine insufficiency (PEI) is one of the most important causes of malnutrition and weight loss in these patients. The prevalence and clinical consequences of PEI in APC are poorly investigated with heterogeneous results. We sought to determine the prevalence and clinical consequences of PEI, and effect of pancreatic enzyme replacement therapy (PERT) in patients with APC by systematic review and meta-analysis.

Aims & Methods: Scopus, Medline and Embase were searched for cohort studies or randomized clinical trials reporting PEI and/or the effect of PERT in patients with APC. We considered PEI as an abnormal result on direct and/or indirect pancreatic exocrine function tests. PERT was evaluated by its effect on survival and quality of life (QoL) in patients with APC.

Results: A total of 11 studies were included; 7 studies reported the prevalence of PEI and 7 the effect of PERT in APC. Pooled prevalence of PEI in APC was 72% (95% confidence interval (CI): 55-86%), resulting significantly higher when tumours were located in the pancreatic head (RR= 3.36, 1.07-10.54; P= 0.04) 6 studies investigated the impact of PERT on survival/QoL. PERT was associated with 3.8 months (95% CI 1.37-6.19) survival benefit. Patients receiving PERT had a trend towards a better QoL.

Conclusion: The prevalence of PEI in APC is substantial and its treatment can improve the outcomes of these patients.

Disclosure: Nothing to disclose

P1106

EARLY PDAC DETECTION: IGF AXIS PROTEIN LEVELS IN PATIENTS WITH NEW ONSET DIABETES AS A USEFUL INDICATOR

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Introduction: Insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 2 (IGFBP-2) are known to be associated with the risk of many cancers. IGF-1 and IGFBP-2 are proteins that belong to the IGF axis, which is involved in glucose and lipid metabolism and may as well promote carcinogenesis.

Aims & Methods: The aim of this study was to evaluate the serum concentrations levels of IGF-1 and IGFBP-2, in patients with newly diagnosed pancreatic adenocarcinoma (PDAC), chronic pancreatitis (CP) and control group with healthy subjects. Their values in diabetes (DM) were also assessed. The study included 83 patients with CP, 92 patients with PDAC and 20 from control group. The concentrations of IGF-1 and IGFBP-2 were estimated by means of ELISA (Corgenix UK Ltd R&D Systems). The study protocol was approved by the Bioethics Committee at the Medical University of Lodz in Poland.

Results: The IGF-1 serum level was significantly higher in CP compared with patients with PDAC (81,11 ± 57,18 ng/ml vs 53,18 ± 36,05 ng/ml, p=0,00041), and both CP patients and PDAC patients were different from controls (81,11 ± 57,18 ng/ml vs 70,66 ± 16,57 ng/ml, p< 0,00001 and 53,18 ± 36,05 ng/ml vs 70,66 ± 16,57 ng/ml, p=0,00027). Patients who had CP without cysts were noted to have a significantly lower level of IGF-1 compared to those with both CP and cysts (60.35±34.68 ng/ml vs 93.55±64.78 ng/ml, p=0,016). IGF-1 in CP without DM was higher compared to IGF-1 in PDAC without DM (91,13 ± 65,48 ng/ml vs 54,75 ± 40,41 ng/ml, p=0,0002). Among patients with CP and DM the IGF-1 was also higher in comparison to patients with PDAC and DM (62,20 ± 32,38 ng/ml vs 48,45 ± 24,88 ng/ml, p=0,049). The serum IGFBP-2 level was significantly higher in CP patients compared to PDAC patients (512,42 ± 299,77 ng/ml vs 301,59 ± 190,36 ng/ml, p=0,000082). In CP and PDAC group the IGFBP-2 serum level was significantly elevated compared to control group (512,42 ± 299,77 ng/ml vs 51,92 ± 29,40 ng/ml, p< 0,00001 and 301,59 ± 190,36 ng/ml vs 51,92 ± 29,40 ng/ml, p< 0,00001). IGFBP-2 in CP without DM was also higher compared to those with PDAC and without DM (559,39 ± 281,43 vs 296,53 ± 196,93, p=0,00001). The results show that at the 0,01 sensitivity level, IGF-1/IGFBP-2 ratio lower than 0,85 points indicates PDAC presence. At this level of sensitivity the test has the specificity of 0,097, (α=0,01; β=0,097; IGF-1/IGFBP-2 ≤ 0,85).

Conclusion: Diabetes accompanying PDAC does not influence the level of IGF-1 as opposed to diabetes in the course of CP. The IGF-1 level can be useful for early diagnosis of PDAC. IGF-1 and IGFBP-2 are good biomarkers of pancreatic diseases, especially CP and PDAC. Elevated levels of IGF-1 in the course of CP may indicate the presence of pancreatic cyst. IGF-1 may be an indicator which signals whether pancreatic diabetes comes from CP or PDAC. Our results show that IGF-1 to IGFBP-2 ratio ≤ 0.85 may be a powerful PDAC indicator. Further studies are necessary to examine if this biomarker will be able to differentiate pancreatic diabetes as a first symptom of PDAC.

Disclosure: Nothing to disclose

P1107

LUNG METASTASIS IN PANCREATIC CANCER: SHOULD STAGING CHEST CT BE ROUTINELY PERFORMED?

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Introduction: National Comprehensive Cancer Network recommend a CT or MRI pancreas protocol for staging of pancreatic ductal adenocarcinoma (PDA). However, CT chest is not mandatory and is deferred to institutional preferences. There is limited data on lung metastasis prevalence in the absence of abdominal metastases in PDA to support these guidelines and to mandate CT chests for complete staging.

Aims & Methods: The primary aim was to analyze our institution's data on PDA patients with primary lung metastasis in the absence of liver metastases. Secondary outcome measures focused on the demographics of the different subgroups of patients with PDA. Data was prospectively collected from May 2013 to July 2018 for patients with PDA who were presented at a multidisciplinary pancreas conference at a tertiary care center. Patients were staged using a CT pancreas protocol and documented as resectable (R), borderline resectable (BR), locally advanced (LA), and metastatic disease. For patients with R, BR, and LA, CT chest results were documented separately. Lung metastasis was determined based on imaging characteristics with MDPC clinical consensus or biopsy results.

	R, BR, LA PDA without lung metastasis n =232	R, BR, LA PDA with lung metastasis n= 19	P value
Sex, Male, n(%)	123 (53.0)	9 (47.4)	0.6390
Age, yrs,			
40-49	6 (2.6)	2 (10.5)	0.0604
50-59	36 (15.5)	3 (15.8)	0.9724
60-69	76 (32.8)	7 (3.7)	0.0083
70-79	72 (31.0)	5 (2.6)	0.0088
80-89	39 (16.8)	2 (10.5)	0.4759
90-99	3 (1.3)	0 (0.0)	0.6178
Race, n(%)			
Caucasian	218 (94.0)	16 (84.2)	0.1021
African American	12 (5.2)	3 (15.8)	0.0620
Hispanic/Latin American	2 (0.9)	0 (0)	0.6786
CA 19-9 level mean, (SD) U/ml	2,289 (13,050)	6,495 (14,808)	0.1825
Lesion Size, Mean (mm)	27.6 (10.1)	31.2 (14.6)	0.1516
Lesion Location, n (%)			
Head	160 (69.0)	14 (73.7)	0.6698
Body/tail	44 (19.0)	3 (15.8)	0.7317
Genu/Neck/Uncinate	24 (10.3)	2 (10.5)	0.9781

[Table 1. Comparison of Demographics and Tumor Characteristics, for patients with R, BR, or LA disease with or without lung metastasis.]

Results: 388 patients were diagnosed with PDA during the study period

where 51 (13.1%) were lost to follow up and the remaining 337 (86.9%) were included in the study. Of these, 74.5% had R, BR, or LA disease while 25.5% had intraabdominal metastasis ($P < 0.0001$). Patients with R, BR, or LA disease had a significantly higher proportion of the PDA arising from the pancreatic head compared to the rest of the pancreas (64.4% vs 35.6%, $P < 0.0001$). 19 out of the 251 (7.6%) patients with R, BR, LA disease were found to have pulmonary metastasis.

Conclusion: Pulmonary metastasis prevalence in PDA patients who had R, BR, or LA disease is clinically relevant to mandate initial staging of pancreatic cancer with a CT of the chest. This could change management decisions for 7.6% of patients.

Disclosure: Nothing to disclose

P1108

DIAGNOSTIC ACCURACY OF FRANSEEN-TIP NEEDLE EUS-FNB IN COMPARISON TO EUS-FNA IN SOLID PANCREATIC LESIONS

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Introduction: The aim of the study is to compare the diagnostic yields of EUS FNA and EUS FNB with 22G Franseen-tip Needle in patients with solid pancreatic masses.

Aims & Methods: We've analyzed data from 60 patients with solid pancreatic lesions, who underwent EUS guided tissue sampling with FNA 22-25G or FNB 22G Franseen Tip Needle (Aquire, Boston Scientific) in our centre between November 2018 and November 2019. The number of needle passes in every procedure was exclusively related to endoscopist's opinion (not standardized). Biopsy specimens were evaluated by experienced pathologist, blinded to the sampling technique. Rapid on-site evaluation was not available. The final diagnosis was confirmed by surgical specimen, follow-up (clinical evaluation) and/or a second biopsy. Data was analysed in a prospective manner and diagnostic yield of FNA and FNB was compared.

Results: Thirty six patients (20 male) underwent FNA puncture, 24 (14 male) were assessed with the FNB technique. Chronic pancreatitis was present in 18% (11/60) of the patients. Tumors' average size was 37 mm in the FNA Group and 30 mm in FNB group ($p > 0.05$). The specificity and sensitivity for FNA were 96% and 82%, and for FNB 100% and 92% ($p > 0.05$). Based on final diagnosis FNB technique was accurate in 92% vs. 82% in FNA group; $p > 0.05$. The average count of needle passes per patient was fewer in the FNB group compared to the FNA group (2.8 vs. 3.5, $p < 0.05$). Further, in 69.23% of cases FNB provided histological specimen with preserved architecture, compared to 40.6%, in FNA $p < 0.05$. Post-biopsy complications were not detected in both groups.

Conclusion: FNA and FNB provide equivalent accuracy in the diagnosis of pancreatic tumors with equivalent safety profile. FNB performs better in ensuring informative tissue specimen with fewer needle passes needed.

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P1109

PHASE II CLINICAL TRIAL USING NOVEL PEPTIDE COCKTAIL VACCINE AS A POSTOPERATIVE ADJUVANT TREATMENT FOR SURGICALLY RESECTED PANCREATIC CANCER PATIENTS

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Introduction: Therapeutic cancer vaccines have the efficacy and good tolerability, which are distinct from chemotherapy or radiotherapy. A previous phase II/III trial using a single cancer peptide vaccine derived from vascular endothelial growth factor receptor (VEGFR)2 for patients with advanced pancreatic cancer did not demonstrate the overall survival (OS) benefit (Yamaue et al. Cancer Sci 2015). However, for the next trial, we conducted a multicenter phase II study using multi-peptide cocktail vaccine named OCV-C01 derived from a novel higher immunogenic antigen KIF20A, VEGFR1 and VEGFR2 combined with gemcitabine in postoperative adjuvant setting.

Aims & Methods: We conducted a multicenter phase II study using OCV-C01 with the aim to estimate the disease-free survival (DFS) and to explore the predictive biomarkers associated with this immunotherapy treatment. At each 28-day treatment cycle, patients received weekly subcutaneous injection of OCV-C01 for 48 weeks, and gemcitabine was administered intravenously at 1,000 mg/m² on days 1, 8, and 15 for 24 weeks. Patients were followed for 18 months. The primary endpoint was disease-free survival (DFS) and secondary endpoints included safety, overall survival (OS) and immunological assays on peptide-specific cytotoxic T lymphocyte (CTL) activity and KIF20A expression in resected pancreatic cancer.

Results: The median DFS was 15.8 months (95% confidence interval (CI), 11.1-20.6), and the DFS rate at 18 months was 34.6% (95% CI, 18.3-51.6). The median OS was not reached and the OS rate at 18 months was 69.0% (95% CI, 48.8-82.5). The administration of OCV-C01 was well tolerated. In the per protocol set, there were significant differences in DFS between patients with and without KIF20A-specific CTL responses ($p=0.027$), and between patients with and without KIF20A expression ($p=0.014$). In addition, all four patients who underwent R0 resection with KIF20A expression had no recurrence of pancreatic cancer with KIF20A-specific CTL responses.

Conclusion: OCV-C01 combined with gemcitabine was tolerable with a favorable median DFS of 15.8 months. In cancer vaccine treatment, positive expression of targeted antigen was essential, and postoperative adjuvant setting was more suitable than advanced state of cancer.

Disclosure: Nothing to disclose

P1110

COMPARISON OF SURGERY AND CHEMOTHERAPY IN THE TREATMENT OF PANCREATIC CANCER WITH PREOPERATIVE LYMPH NODE METASTASIS

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Introduction: Pancreatic cancer is a fatal disease. The oncological results of curative surgery alone are disappointing, owing to the high frequency of relapses or surgical complications. In particular, the prognosis of patients with pathological lymph node metastasis after pancreatectomy is reported to be significantly poorer than that of patients without lymph node metastasis. On the other hand, chemotherapy for unresectable pancreatic

cancer is evolving. Therefore, if lymph node metastasis is suspected, we should carefully consider whether pancreatectomy is the best treatment. There are many reports based on postoperative staging; however, reports about the prognosis of patients with preoperative lymph node metastasis in pancreatic cancer are few. In this study, we aimed to compare the prognosis of chemotherapy (or chemoradiotherapy) with that of surgery in cases of preoperative lymph node metastasis.

Aims & Methods: Between April 2009 and April 2019, 125 pancreatic cancer patients with no distant metastasis but with lymph node metastasis (clinical N1 or N2 M0; cN1 or N2 M0) were enrolled. Forty-one patients with best supportive care and 20 who underwent neoadjuvant chemotherapy were excluded. We retrospectively compared the overall survival (OS) of chemotherapy (or chemoradiotherapy) with that of surgery. Survival data were compared using a log-rank test. P -value < 0.05 was considered statistically significant. Clinical staging was determined by the Union for International Cancer Control (UICC) TNM classification (The 8th Edition). Preoperative workup was performed with multidetector computed tomography using a standard protocol optimized for pancreatic tumors.

Results: Twenty-two patients were included in the chemotherapy (or chemoradiotherapy) group, and 42 patients were included in the surgery group. In the two groups, no significant difference was observed in the background factors such as sex, age, location, and the extent of tumor. The median OS was 11.7 months (95% confidence interval [CI] 11.4-12.2) in the chemotherapy group and 11.6 months (95%CI 6.3-17.1) in the surgery group. There was no significant difference in the two groups (Hazard ratio 1.28 [95%CI 0.73-2.27]; $p=0.39$). Conversely, the 3-year OS rate was 4.5% in the chemotherapy group and 14.2% in the surgery group.

Conclusion: In a case of preoperative lymph node metastasis (cN1 or N2 M0), there was statistically no difference in the median OS between chemotherapy (or chemoradiotherapy) and surgery. However, the surgery group tended to have a slightly higher 3-year OS rate than the chemotherapy group, indicating that a few patients in the surgery group achieved long-term survival through pancreatectomy. Nevertheless, if lymph node metastasis is suspected by preoperative evaluation, pancreatectomy, which is invasive and has many complications, should be selected after careful and appropriate consideration.

Disclosure: Nothing to disclose

P1111

EXPERT REVIEW IDENTIFIES A HIGH PREVALENCE OF “MISSED” PANCREATIC MASSES: A CASE CONTROL TRIAL OF IMAGING IN THE THREE YEARS PRIOR TO A DIAGNOSIS OF PANCREATIC CANCER

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Introduction: Pancreatic cancer (PC) is one of the most lethal cancers worldwide. The overall 5-year survival rate is only around 9%, largely due to the late onset of disease specific symptoms and diagnosis in advanced stages. To improve the treatment options and survival of patients with PC, early detection of PC is critical, since survival rates among patients with smaller lesions (≤ 1 cm) of PC can be high as 100%. Since high quality abdominal cross-sectional imaging is increasingly utilized, we investigated if pancreatic masses were already visible on abdominal CTs performed in patients three years prior to their diagnosis with PC and compared these to a control group of CTs performed in patients without PC and at least 3 year disease-free follow up.

Aims & Methods: One expert abdominal radiologist examined, in a blinded manner, 20 CT scans of prediagnostic PC patients and 80 CT scans of control subjects on specific pancreas findings. Cases were matched with controls in ratio of 1:4 based on age, sex, date (+/-3 months) of imaging and usage of contrast. The exams were annotated as: normal, benign pancreatic disease, suspected pancreatic cystic neoplasm (PCN) or suspected mass. We compared these outcomes with the original radiology report. Sensitivity, specificity and diagnostic odds ratio (95% CI) of the re-assessment by an expert radiologist were calculated based on histological confirmed PC.

Results: On re-examination by an expert radiologist, a pancreatic mass was suspected and urgent additional imaging (< 4 weeks) would have been recommended in 12/20 (60%) of PC cases and 1/80 (1.3%) controls ($P < 0.001$). In the original radiologic report of the cases, the pancreas was considered normal with no need for additional imaging in 14 (70.0%), pancreatitis in 3 (15%), prominent head of the pancreas in 2 (10.0%) and 1 as PCN (5.0%). Additional imaging was recommended by the original radiologist for the cases with pancreatitis and a prominent pancreatic head, but that did not result in a PC diagnosis. In 6/14 (42.9%) PC cases that were unremarkable on the original report; suspicion of a pancreatic mass was raised on re-examination by the expert radiologist. CT-images were obtained with a median of 8 months (IQR 4.3 - 18.5) prior to the PC diagnosis. Demographic data of cases and controls are summarized in Table 2.

Conclusion: There is a high prevalence of suspected pancreatic masses on imaging in the majority of patients who are subsequently diagnosed with pancreatic cancer. However, these lesions are often missed on the initial radiological assessment. There may be a role for augmented intelligence to assist in improving these detection rates, especially when specialty specific expert radiologists are not available.

	PC cases (N = 20)	Controls (N = 80)	p-value
Male (%)*	16 (80.0%)	64 (80.0%)	-
Age (median, IQR)*	69 (63.5 - 78)	69 (63.5 - 78)	-
CT with contrast*	6 (30.0%)	24 (30.0%)	-
Diabetes mellitus	10 (50.0%)	26 (32.5%)	0.008#
Current/former smoker (%)	16 (80.0%)	52 (65.0%)	< 0.0001#
History of alcohol use (%)	4 (20.0%)	7 (8.8%)	0.22#
Family history of PC (1 FDR)	2 (10.0%)	5 (6.3%)	0.62#

* Matched variables, # McNemar's test, PC = pancreatic cancer, CT = computed tomography

[Table 1. Demographics at time of imaging]

Disclosure: M.B. Wallace:Consulting: Virgo Inc, Cosmo/Aries Pharmaceuticals, Anx Robotica (2019), Covidien, GI Supply. Research grants: Fujifilm, Boston Scientific, Olympus, Medtronic, Ninepoint Medical, Cosmo/Aries Pharmaceuticals. Stock/Stock Options: Virgo Inc. Consulting on behalf of Mayo Clinic: GI Supply (2018), Endokey, Endostart, Boston Scientific, Microtek, General payments/Minor Food and Beverage: Synergy Pharmaceuticals, Boston Scientific, Cook Medical.

P1112

PILOT COMPARISON BETWEEN NOVEL HYBRID AND DRY SUCTION TECHNIQUES FOR ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE BIOPSY IN PANCREATIC SOLID LESIONS: A PROSPECTIVE, SINGLE-BLIND, RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) has been widely applied. However, there is no clear consensus on the optimal biopsy technique.

Aims & Methods: We describe a novel hybrid suction technique (NHST) with an aim to compare the efficacy and safety between NHST and the dry suction technique (DST) in pancreatic solid lesions. In this prospective, randomized, crossover, blinded study, patients with suspected pancreatic malignancy were randomized to the DST (group A) versus the NHST (group B) for the first pass, and the two techniques were performed alternately. EUS-FNB was performed using a 22-gauge ProCore needle. The primary outcome was the comparison of specimen adequacy and diagnostic yields between NHST and DST. Secondary outcomes included the macroscopic visible core (MVC) length, blood contamination of specimens, and adverse events of the two techniques.

Results: From January 2019 to September 2019, 54 consecutive patients presenting for EUS with possible FNB of pancreatic solid lesions were offered the chance to participate in the study. Among them, 4 patients were excluded because of the solid-cystic lesion in 3 and needle tip bending after performing 2 passes in 1. The remaining 50 patients (16 women) with a median age of 60 years (IQR, 49-67.25 years) were included in the final analysis. A total of 216 passes with a median pass of 4 (IQR, 4-5) were performed. The specimen adequacy of NHST was significantly higher in "per lesion" ($P=0.026$), "per pass" (cytopathology: $P=0.034$; histopathology: $P=0.042$), and first-pass ($P=0.034$) analysis compared with DST. Comparisons of diagnostic yields showed significantly superior histopathological ($P=0.014$) and first-pass (kappa: NHST: 0.743, DST: 0.519) diagnostic yields in NHST than in DST. MVC lengths were 8 mm (interquartile range [IQR]: 3.25-15mm) for NHST and 10 mm (IQR: 5.25-15mm) for DST ($P=0.036$). Blood contamination was significantly more serious in DST than in NHST (cytopathology: $P=0.021$; histopathology: $P=0.042$). There was a bleeding case after NHST.

Conclusion: EUS-FNB with NHST resulted in significantly better quality of specimen, histopathological and first-pass diagnostic yields, and comparable safety when compared with the DST. Thus, NHST is preferred for EUS-FNB in pancreatic solid lesions.

Disclosure: Nothing to disclose

P1113 WITHDRAWN

P1114

POSITIVE PREDICTIVE VALUE OF MAIN PANCREATIC DUCT DILATION FOR MALIGNANCY PREDICTION IN SOLID PANCREATIC MASSES: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Introduction: Main pancreatic duct dilation (MPD) could represent an indirect sign of the presence of a neoplastic lesion growing into the duct. However, other conditions could be related to MPD dilation, such as chronic pancreatitis, mucous secretion from intrapapillary mucinous neoplasms, or periampullary masses that cause obstruction. **Aim:** to evaluate the association between main pancreatic duct (MPD) dilation and malignancy occurrence in pancreatic solid lesions during endoscopic ultrasound (EUS).

Aims & Methods: Retrospective data from consecutive patients (Jan/2016 to Dec/2018) with solid hypoechoic pancreatic lesions on EUS was prospectively analyzed. The MPD diameter were measured in all patients. All solid lesions were punctured via fine-needle aspiration for histological analysis. Malignancy was defined in accordance with histological, surgical specimen and/or 6-months follow up. MPD diameter cut-off value for malignancy was estimated using Youden's index. A sub-analysis in accordance with lesion localization, MPD diameter, EUS and EUS-guided fine-needle aspiration biopsy for determining sensitivity, specificity, positive and negative predictive values (PPV/NPV) for malignancy was calculated. Data was analyzed in Rv.3.6.0.

Results: 114 patients with pancreatic hypoechoic lesions were included for analysis. The mean age was 64.7 ± 14.4 years, and 49.6% female. Most lesions were in the head of the pancreas (76.5%) or uncinate process (8.4%), with a median size lesions of 34 mm (range: 10 - 70). According to histology, 80.7% patients had malignant lesions, follow up confirmed malignancy in 101/114 (88.5%). The median pancreatic duct diameter was 4.0 mm (range: 1.2 - 13.0) in the malignant group and 4.2 mm (range: 1.3 - 7.0) in the non-malignant lesions (p=1.000). For both head and overall pancreatic lesions, an MPD diameter cut-off value >5.2 mm as a marker of malignancy was estimated.

According to our results, sensitivity, specificity, PPV and NPV for determining malignancy through MPD diameter >5,2 mm was: 25%, 89%, 95%, and 12%, respectively; overall EUS: 93%, 77%, 97% and 59%, respectively; for EUS-guided fine-needle aspiration biopsy: 95%, 100%, 100% and 72%, respectively.

Conclusion: A dilated MPD diameter >5.2 mm in the context of solid pancreatic masses represents a useful indirect parameter for suspected malignancy.

Disclosure: Dr Robles Medrand C is a key opinion leader for Pentax Medical and Boston Scientific. The other authors have nothing to disclose.

P1115 WITHDRAWN

P1116

[¹⁸F]FDG-PET/CT AND LONG-TERM RESPONSE TO EVEROLIMUS IN ADVANCED NEUROENDOCRINE NEOPLASIA

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Introduction: In the last few years, ¹⁸F-fluorodeoxyglucose PET/CT (FDG-PET) has emerged as an important tool to define tumor aggressiveness and give relevant prognostic information, with several studies investigating its role in the diagnostic approach and during the follow-up of NENs. However, although a positive correlation between FDG-PET and other well-known predictors of response to anti-tumor therapy as Ki67 has been demonstrated (13, 14), the ability of this diagnostic tool to predict treatment efficacy is not well established. Furthermore, the possible impact of positive FDG-PET on everolimus efficacy remains unclear.

Aims & Methods: This study aims to identify, in advanced progressive NENs treated with everolimus, potential correlation between FDG-PET findings and response to therapy in search of a predictor of long-term efficacy. Retrospective analysis of patients with sporadic, advanced, progressive NEN treated with everolimus, with available data on FDG-PET before commencing therapy. Data is expressed as median (25th - 75th IQR). Risk factor analysis and survival analysis are performed by logistic regression and Cox proportional-hazard regression and Kaplan-Meier curves, as appropriate.

Results: A total of 66 patients, including 35 females, with median age 58 yr (IQR 47 - 66) were included. In the majority of pts, the primary tumor was located in the pancreas (n=37, 56%), and had a G2 grading (n=50, 75.7%). 97% had stage IV disease, liver metastases being present in all these patients. Overall, 20 patients (30.3%) had a functioning tumor (carcinoid syndrome n=16, 24.2%). The majority of patients (n=60, 90.1%) had positive ⁶⁸Ga-DOTA-NOC PET, whereas 30 patients (45.4%) had positive FDG-PET. Specifically, FDG-PET was homogeneously positive in all tumor lesions in 19 patients (28.8%), whereas it was heterogeneously positive (with coexisting positive and negative tumor lesions) in the remaining 11 patients (16.7%). In patients with positive FDG-PET, median SUV was 6 (4 - 7.5). Among FDG-PET positive patients, 24 had NET G2 (80%), 3 had NET G3 (10%), and 3 NET G1 (10%). Overall, disease stabilization and partial response were obtained in 71.2% and 6% of patients, respectively. Long-term response (> 24 months) was observed in 33% of patients. Ki67 was the only predictor for tumor progression (p=0.03). The proliferative index Ki67 was the only factor significantly associated with an increased risk of disease progression during everolimus treatment, HR being 1.05 for each increasing unit (p=0.023). Conversely, no difference in terms of risk of DP was observed according with primary tumor site, FDG-PET finding, and ECOG performance status at time of treatment initiation. Similar PFS probability was observed in NET G1 compared with NET G2, median PFS being 28 months and 20 months, respectively (p=0.277). In addition, similar PFS probability was observed in patients with negative FDG-PET compared with those with positive FDG-PET (median PFS were 24 months and 18 months, respectively; p= 0.337).

Conclusion: Everolimus is a valid therapeutic option for advanced, progressive, well-differentiated NENs, even in those patients with positive FDG-PET.

Physicians should be reassured not to debarring patients of the everolimus therapeutic option basing on the sole positivity of this imaging procedure, since it remains a valid treatment with relevant probability to achieve long-term disease control over time, particularly in G1 and G2 NENs with low SUV at FDG-PET.

Disclosure: Nothing to disclose

Poster presentations

Endoscopy and imaging

Poster Presentations Endoscopy and imaging

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Endoscopy and imaging

09:00-19:00 / Poster Exhibition

P1117 WITHDRAWN

P1118

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT IN CHILDREN: A SINGLE-CENTER EXPERIENCE

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Introduction: Insertion of a percutaneous endoscopic gastrostomy (PEG) is a common indication to provide safe intragastric nutritional support in children with different conditions requiring prolonged enteral tube feeding.

Aims & Methods: The aim of this study was to evaluate the nutritional status improvement and complications rates in children who had undergone PEG during the last 3 years in our Pediatric Gastroenterology Department. **Methods:** The anthropometric data, indications, complications and follow-up findings of the patients who had undergone PEG between 2017-2020 were examined retrospectively using patients electronic files.

Results: 72 PEG procedures were performed during 3 years. All PEG were performed by an experienced pediatric gastroenterologist and a pediatric surgeon using the pull-through technique under general anesthesia. A single dose of cephalosporin was prescribed for all cases before procedure. The indications for PEG were: neurologic disorders (58), metabolic conditions associating dysphagia (n = 8), severe malnutrition caused by chronic renal failure, congenital heart diseases or malignancies (n = 6). The median age of the patients was 2.85 years (5 months-17 years) and the mean body weight was 12.58±7.8 kg. Before PEG placement, the mean weight z score was -2.87±1.2 and the mean height z score was -2.85±0.46. The follow-up mean weight and height Z scores at one year after procedure significantly increased to -1.58±0.6 (p< 0.005) and -1.62±0.4 (p< 0.005) respectively. Minor complications developed in 9 patients (12.5%), including 6 mild peristomal infections (8.3%), 2 overgranulation at the gastrostomy site (2.7%) and one gastric leakage (1.3%). In 2 patients (2.7%) major complications occurred represented by aspiration and pulmonary infection. There were no deaths related to PEG.

Conclusion: PEG provides significant improvement of nutritional status in children requiring long-term tube feeding. This is a safe procedure with high efficacy. Although minor complications may occur in up to 12.5% of patients, there is a low rate of severe complications, so this procedure should be performed more often, even in infants with severe conditions.

Disclosure: Nothing to disclose

P1119

PERORAL ENDOSCOPIC TUMOR RESECTION WITH PRESERVED MUCOSA (POET-PM) TECHNIQUE FOR MANAGEMENT OF UPPER GASTROINTESTINAL TRACT SUBEPITHELIAL TUMORS

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Introduction: The incidence of upper gastrointestinal tract subepithelial tumors (UGI-SETs) is increasing and differentiation between benign and malignant nature of small UGI-SETs is a clinical conundrum to endoscopists.

Aims & Methods: This study aimed to investigate peroral endoscopic tumor resection with preserved mucosa (POET-PM) technique for treatment of UGI-SETs.

Between February 2011 and September 2019, consecutive patients with SETs of esophagus, stomach and duodenum who underwent POET-PM for enlarging size during follow-up, malignant features or by patients' requests were enrolled. Demographic, endoscopic and pathological data were analyzed retrospectively.

Results: Totally 14 esophageal, 24 gastric and 4 duodenal SETs were resected. The mean (±SD) age, gender ratio, endoscopic/pathological tumor size, complete resection rate, hospital stays, and mean procedure time of esophageal, gastric and duodenal SET patients were 53 (±13), 49.75 (±2.73), and 49.75 (±5.50) years old, female-to-male ratio of 35.71%, 54.17% and 0%, 12.36 (±9.89)/9.86 (±4.67), 12.17 (±5.55)/12.25 (±5.60), and 9.00 (±1.15)/7.50 (±1.00) mm, 92.9%, 87.5% and 75%, 4.14 (±0.21), 4.17 (±0.20), and 4.25 (±0.25) days, 13.86 (±6.05), 39.21 (±13.29), and 37.00 (±10.61) minutes, respectively. The overall complication rate was 11.9%, including 3 fever and 2 pneumoperitoneum with all self-limited. There was no mortality or recurrence reported with mean follow-up period of 23.74 (±4.12) months.

Conclusion: POET-PM is a safe and efficient third space endoscopic resection technique for UGI-SETs less than 20mm. Long term data are warranted to validate these results.

Disclosure: Nothing to disclose

P1120 WITHDRAWN

P1121 WITHDRAWN

P1122 WITHDRAWN

P1123 WITHDRAWN

P1124

A CASE SERIES OF USING “FISHING TECHNIQUE” IN PREVENTING ESOPHAGEAL STENT MIGRATION

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Introduction: Esophageal stenting is an effective non-surgical treatment in treating many esophageal diseases. However, esophageal stent migration is not uncommon and risk can be up to 35%, especially in cases of benign esophageal diseases without an anatomical stenosis or stricture for stent anchoring. A novel technique - “Fishing Technique” was used by our team to prevent stent migration.

Aims & Methods: We hereby report our experience in using “Fishing Technique” in preventing esophageal stent migration. In a series of cases of benign esophageal disease with stent insertion, “Fishing Technique” was used to prevent stent migration. A “fishing rod” was first prepared using a Vicryl-O suture to make a Vicryl-O loop at the tip of a Ryle’s tube. After deploying the esophageal stent to its optimal position, the “fishing rod” was inserted through patient’s nostril down to the proximal end of the stent. Endoscopic clips, acting as “fishing hook”, were then applied to appose the Vicryl-O loop to the proximal flange of the stent. The external part of Ryle’s tube was fixed to patient’s nose and face at two different points to prevent stent migration. An external marking was made using marking pen at the Ryle’s tube at nostril level, acting as a “buoy”, to detect any migration of the whole system clinically. When removal of stent was indicated, endo-scissors were used to cut open the Vicryl-O loop. The Ryle’s tube and the stent were removed as usual.

Results: From April 2019 to February 2020, “Fishing Technique” was applied to 3 cases in our hospital. First case was a patient with Boerhavie disease with post-operative leakage. Second case was a patient with post-total gastrectomy esophagojejunostomy leakage. Third case was a patient with post-esophagectomy gastric tube stapler line leakage. Post-stenting chest radiography confirmed all stents were in optimal position. There was no stent migration observed clinically using external marking at Ryle’s tube and radiologically in chest radiography. After stent removal, all defects healed with endoscopic and fluoroscopic confirmation.

Conclusion: “Fishing Technique” is an effective method in preventing esophageal stent migration using material easily available in clinical area. It allows 2-point fixation of stent externally and clinical detection of stent migration. The stent can be removed easily using usual endoscopic technique.

Disclosure: Nothing to disclose

P1125

OUTCOMES OF ENDOSCOPIC AND SYMPTOM SCREENING EVALUATION AFTER AF ABLATION TREATMENT: RESULTS FROM THE IMPACT STUDY

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Introduction: Catheter ablation treatment for atrial fibrillation (AF) is performed for an increasing number of patients worldwide per annum. Risk of severe oesophageal thermal injury is a well-known serious complication,

and potentially limits the applicability of AF ablation. Both radiofrequency and cryotherapy thermal energy ablation aim to create transmural atrial myocardial wall lesions and in doing so may also inflict collateral structural damage to the oesophageal wall and its surrounding vagal plexus. The risk of fatality is high in those that develop atrio-oesophageal fistula and little is known about the long-term outcomes in those who sustain lower grades of injury, which may include gastroparesis. Up till now, no strategies to limit oesophageal injury have been successful. Controlled oesophageal cooling is a non-mechanical method to protect the oesophagus from this form of iatrogenic trauma. The effect of controlled oesophageal cooling with modern ablation treatment technology has not been previously studied.

Aims & Methods: Aims: To investigate the outcomes patients who receive AF ablation treatment with and without oesophageal cooling protection.

Method: The IMPACT study was a double-blind randomized controlled trial studying the effect of controlled oesophageal cooling for oesophageal protection during AF ablation. There was 1:1 randomization to a control group of standard practice utilizing a single-sensor temperature probe. In the study group, the device was used to keep the luminal temperature at 4°C during radiofrequency (RF) ablation for AF. Endoscopic examination was performed post-ablation at a timing of 7-14 days by one of two expert endoscopists and oesophageal injury was graded using a modified scoring system. The patient and the endoscopist were blinded to the randomization. Clinical follow up occurred 3 months post-ablation, with completion of structured questionnaires (GERD-Q and GCSI); both patient and follow up clinician were blinded.

Results: We recruited 188 patients, of whom 120 underwent endoscopy. Thermal injury to the oesophageal mucosa was significantly more common in the control group than in those receiving oesophageal protection (12/60 versus 2/60; P=0.008). The majority of those who passed through the 1st follow up evaluation (n=118) did not experience gastrointestinal or chest pain symptoms and there was no difference between the randomized groups. Only 4.3% overall had severe symptoms and they were poorly correlated against those who sustained mucosal lesions but strongly in endoscopically detected gastroparesis. Gastroparesis was more common in the control group with a trend towards significance (2/60 versus 6/60; P=0.27). A significant GERDQ score was reached in 4/72 patients in control group versus 0/64 in the protected group; p=0.12. A significant GCSI score was reached in 4/72 patients in control group versus 2/64; P=0.68 and endoscopy findings were consistent with gastroparesis. Endoscopy findings did not report any transoesophageal echo probe or EnsoETM device-related trauma.

Conclusion: Controlling the luminal oesophageal temperature during AF ablation can lower the risk of oesophageal thermal injury. Patient symptoms correlate poorly against those who sustain oesophageal mucosal injury but are consistent to those who develop vagal plexus injury. Longer duration of follow up is required to assess the clinical significance of this category of iatrogenic lesions.

Disclosure: Dr Leung has received research support from Attune Medical (Chicago, IL). Dr Gallagher has received research funding from Attune Medical and has acted as a consultant and a paid speaker for Boston Scientific and Cook Medical.

P1126

THE REAL-LIFE DIAGNOSTIC ACCURACY OF REGULAR ARRANGEMENT OF COLLECTING VENULES IN DETECTING *H. PYLORI*-NEGATIVE PATIENTS

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Introduction: The identification of regular arrangement of collecting venules (RAC) has been suggested as an accurate tool for detection of *H. pylori*-negative patients. Since most studies use strict in- and exclusion criteria, our aim was to provide real-life data on the diagnostic accuracy of RAC-positivity (RAC+) in identifying *H. pylori*-negative patients.

Aims & Methods: Data from all gastroduodenoscopies with biopsies for *H. pylori*-screening were collected prospectively from September 2019 onwards, until March 2020. In comparison to previous work, no age or medication restrictions were used. A history of (distal) gastrectomy or gastric bypass, and/or poor visibility were the sole exclusion criteria. Patients were regarded as RAC+ when diffuse star-like venules were identified on the lesser curvature. If absent or only patchy, patients were considered RAC-negative (RAC-). *H. pylori*-status was confirmed by samples in the gastric body (2) and antrum (2). Pathologists were blinded to the RAC-status.

Results: In total, 205 consecutive patients were included (49.8% female, mean age 58 years (IQR 45-72). Twenty-one patients (10.2%) were *H. pylori*-positive, all of which were RAC-. Compared to RAC+ patients (n=59), RAC-patients (n=146) were older (20.3% vs. 44.5% ≥65 years, p< 0.001) and were treated more often with PPIs (49.2% vs. 65.1%, p=0.041), anti-coagulants (8.5% vs. 19.9%, p=0.061) and NSAIDs (0% vs. 7.5%, p=0.036). Most importantly, all RAC+ patients were *H. pylori*-negative, resulting in a sensitivity and NPV of 100%, yet low specificity (32.1%), PPV (14.3%) and diagnostic accuracy (39.0%). Reduced rates of RAC+ were seen amongst patients receiving PPIs (OR 0.52 [95% CI 0.28-0.96], p=0.036), NSAIDs (OR 0.10 [95% CI 0.01-1.71], p=0.112) and anticoagulants (OR 0.37, [95% CI 0.14-1.02], p=0.054).

Conclusion: Our real life data suggest that RAC+ has great sensitivity for the detection of *H. pylori*-negative patients, at the expense of a poor specificity and PPV. Compared to historical data, lower rates of RAC+ were seen, which can be attributed to a relatively high percentage of patients treated with PPIs, NSAIDs and anticoagulants.

Disclosure: Nothing to disclose

P1127

MEASUREMENT OF INTRAGASTRIC PRESSURE DURING STRONG EXTENSION OF THE GASTRIC WALL DURING ENDOSCOPY: A PROSPECTIVE STUDY

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Introduction: Extension of the gastric wall is important in endoscopic screening for early gastric cancer. If the gastric wall is not fully distended by insufflated air, the area behind the folds in the greater curvature of the gastric corpus becomes a blind spot. In addition, accurate diagnosis of invasion depth of early gastric cancer is important when deciding the indications of endoscopic intervention. We previously reported that the “non-extension sign” is useful in the diagnosis of invasion depth of early gastric cancer and indicated that any evaluation must be conducted when the gastric wall is strongly extended, in order to facilitate accurate diagnosis[1]. However, the optimal intragastric pressure required for strong extension of the gastric wall is unclear. This pilot study aimed to determine the optimal intragastric pressure required to achieve strong extension of the gastric wall.

Aims & Methods: **Aims:** This pilot study aimed to determine the optimal intragastric pressure required to achieve strong extension of the gastric wall.

Methods: Participants were consecutive patients who underwent upper gastrointestinal endoscopy between January and March 2019. The intragastric pressure at the time of strong expansion of the gastric wall was measured. The time of strong expansion of the gastric wall was defined as the time when the gastric wall was sufficiently extended by insufflated air to the extent that the folds in the greater curvature of the gastric corpus were flattened during upper gastrointestinal endoscopy. The measurement was performed using a pressure measurement device directly connected to the hole of the forceps channel that we had developed.

Results: A total of 51 patients were analyzed. The mean ± standard deviation of intragastric pressure was 14.7 ± 3.6 mmHg. It was found that strong extension of the gastric wall was achieved when the intragastric pressure was set at 20 mmHg in 96.1% (49/51) of the patients.

Conclusion: The results show that strong extension of the gastric wall can be achieved in almost all patients when the intragastric pressure is set at 20 mmHg.

References: 1) Nagahama T, Yao K, Imamura K, et al. Diagnostic performance of conventional endoscopy in the identification of submucosal invasion by early gastric cancer: the “non-extension sign” as a simple diagnostic marker. *Gastric Cancer*. 2017; 20: 304-313.

Disclosure: Nothing to disclose

P1128

THE ESTIMATED CONTAMINATION RATE OF REPROCESSED GASTROSCOPES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Reusable flexible gastroscopes are challenging to reprocess properly and appropriate reprocessing is essential to assure quality and patient safety. Multiple studies have found that there is a risk that reprocessed patient-ready gastroscopes remain contaminated even when following reprocessing guidelines, which increases the risk of patients acquiring an endoscope-associated infection.

Aims & Methods: This study aimed to estimate the contamination rate of reusable patient-ready gastroscopes. A systematic literature review was conducted in PubMed and Embase to identify studies, in which gastroscopes have been cultured for microbiological growth after reprocessing. The publication date for the studies was from January 2010 to May 6, 2020. Only full-text papers on randomized controlled trials and observational studies were included. Publication languages included English and the Scandinavian languages. Both thesaurus and free-text searches were performed. Only studies with a sample size of 10 samples or more were included to estimate the contamination rate. The outcome of the random effects model was a pooled contamination rate of patient-ready reusable gastroscopes based on each included study. Inconsistency index (I^2) statistics were used to analyze inter-study heterogeneity and publication bias was assessed using Egger's regression test and funnel plots.

Results: In the systematic literature review, 2,071 studies were found via PubMed and 1,624 studies via Embase. After applying the inclusion and exclusion criteria, the search was narrowed down to 45 studies which were reviewed in full detail. Five studies met the inclusion criteria and the total sample size included 524 samples from gastroscopes, of which 97 were contaminated. Studies were excluded if they did not state the total number of samples from the gastroscopes and the number of which that were contaminated. Included studies were conducted in the United States, Canada, Brazil, Taiwan, and China. The pooled contamination rate was 22.31% +/- 0.061 (95% CI: 0.1021 - 0.3340). I^2 was 66.54% which was considered moderate heterogeneity. Egger's regression test was significant for publication bias ($p < 0.01$).

Conclusion: The contamination rate of patient-ready reusable gastroscopes was estimated to be 22.31% based on currently available literature. Significant publication bias and a small sample size should be considered. More high-quality studies should be performed to investigate the true contamination rate of reprocessed gastroscope more thoroughly and to assess the infection risk associated with contaminated gastroscopes.

Disclosure: Sara Larsen is employed by Ambu A/S, Ballerup, Denmark

P1129

BIOPSY SAMPLING IN UPPER GASTROINTESTINAL ENDOSCOPY - A SURVEY FROM TEN TERTIARY REFERRAL CENTRES ACROSS EUROPE

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Introduction: National and international guidelines give robust recommendations on which biopsies should be taken in the presence of endoscopic signs of gastric inflammation as well as with other indications. Nevertheless, adherence to these guidelines often seems to be arbitrary.

Aims & Methods: This study aimed to give an overview on current practice in tertiary referral centres across Europe.

Data was prospectively collected at ten tertiary referral centres across Europe. In addition to demographic data, the indication for each procedure was recorded as well as what biopsies were taken and the endoscopic findings. Findings were compared between centres and factors influencing the decision to take biopsies were explored.

Results: A total of 9425 gastroscopies were analysed. Biopsies were taken in 56.6% of procedures with significant variation between centres ($p < 0.001$). Sampling location varied dependent on the indication for the procedure ($p < 0.001$), but there was no consistent pattern across the participating centres.

If investigation of iron deficiency anaemia was the indication for the gastroscopy, duodenal samples were taken in 48.7% and samples from both gastric antrum and body in 32.6% of procedures. Interestingly, less biopsies were taken in centres routinely applying the updated Sydney classification for gastritis assessment or the OLGA staging system compared to centres where this was done only upon request ($p < 0.001$).

More biopsies were taken in centres following the MAPS guidelines on stomach surveillance ($p < 0.001$). Although the patients' age had no influence on the decision to take biopsies in the whole cohort ($p = 0.537$), in 8 centres biopsy sampling was significantly more likely in younger patients

($p < 0.05$). The percentage of procedures with biopsies correlated directly with additional costs charged per procedure in case of biopsies at the respective centres ($r = 0.709$, $p = 0.022$).

Conclusion: In general, adherence to guideline recommendations for biopsy sampling at gastroscopy seems to be inconsistent across the participating centres. Our data suggest rather centre-specific policies.

Disclosure: Nothing to disclose

P1130

A NOVEL ULTRATHIN ENDOSCOPE WITH TAPERING BODY STIFFNESS IN SHORTENING ESOPHAGOGASTRODUODENOSCOPY EXAMINATION TIME

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Introduction: Ultrathin endoscopes are commonly used for surveillance esophagogastroduodenoscopy (EGD) to reduce discomfort associated with scope insertion. However, the flexibility of an ultrathin endoscope is a trade-off between reducing discomfort and lengthening examination time.

Aims & Methods: EG17-J10 (EG17) is a novel ultrathin endoscope characterized by its tapering body stiffness; however, the flexibility of its tip is comparable to that of the traditional ultrathin endoscope EG16-K10 (EG16). We compared EGD examination time between EG17 and EG16. A total of 319 examinees who underwent EGD from November 2019 to January 2020 at the Chiba-Nishi General Hospital were enrolled. Six examinees were excluded due to past history of surgical resection of the upper gastrointestinal tract or too much food residues; 313 examinees (EG17, 209; EG16, 104) were retrospectively analyzed. The examination time was divided into three periods: esophageal insertion time (ET), gastroduodenal insertion time (GDT), and surveillance time of the stomach (ST). The total amount of ET, GDT, and ST was defined as total examination time (TT).

Results: No significant differences were found between age (63.0 ± 13.8 vs. 63.3 ± 12.7 years), gender (male/female: 117/92 vs. 64/40), and use of sedation agent (143/66 vs. 65/39). TT of EGD using EG17 was significantly shorter compared to EGD using EG16 (222.7 ± 68.9 vs. 245.7 ± 78.5 seconds) ($p = 0.004$). Among the three periods of examination time, ET (66.7 ± 24.1 vs. 76.0 ± 24.1 seconds) ($p = 0.001$) and GDT (47.9 ± 17.4 vs. 55.2 ± 35.2 seconds) ($p = 0.007$) of EGD using EG17 were significantly shorter compared to EGD using EG16, except for ST ($108.1 \pm 51.5.1$ vs. 114.5 ± 50.1 seconds) ($p = 0.148$).

Conclusion: An ultrathin endoscope with tapering body stiffness can shorten EGD examination time, mainly due to the shortening of insertion time.

Disclosure: Nothing to disclose

P1131

PREDICTORS OF FAILURE OF ENDOSCOPIC HEMOSTASIS IN PATIENTS WITH SEVERE PEPTIC ULCER BLEEDING

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Introduction: Overall mortality in patients with upper GI bleeding remains between 6%-14%. Risk factors for peptic ulcer disease are well known. However, these risk factors may not be predictive factors for hemostatic therapy.

Aims & Methods: **Aim:** To identify predictive factors for failure of endoscopic hemostasis.

Methods: Single-center retrospective analysis of patients presented with peptic ulcer bleeding between Jan 2007 and Feb 2016. Patients who had re-bleeding (group A) were compared to patients without re-bleeding (group B). Furthermore, a subgroup of patients that required coil embolization to achieve hemostasis was analyzed using matched-pair analysis. The groups were compared regarding sex, age, ulcer size, ulcer number, predisposing factors, clinical presentation, the type of endoscopic intervention and comorbidities.

Results: In total 18816 upper endoscopies were performed. Peptic ulcer bleeding was detected in 754 patients (4%). Bleeding from solitary ulcers was most frequently found (64.46%). Forrest Ib ulcers were most commonly detected (182 pts. (24.14%)). The most seen predisposing factor was aspirin intake (288 pts. (38.20%)) followed by H. pylori infection (267 pts. (35.41%)), NSAIDs use was noted in 115 pts. (15.25%) and anticoagulants in 179 pts. (23.74%). The combination of H. pylori and aspirin was the most frequent one but was found only in 93 pts. (12.33%). Epinephrine injection was used in 323 pts. (42.84%) followed by clip therapy in 260 pts. (34.48%). Re-bleeding occurred in 110 pts. (14.58%). We identified the following risk factors for re-bleeding: age between 60 and 80 years ($p = 0.013$), localization in the antrum ($p < 0.001$), size above 2 cm ($p = 0.040$), anticoagulation therapy ($p = 0.017$) and Forrest types Ib, Ia IIa ($p < 0.001$). Hemostasis was achieved using endoscopic therapy in 391 pts. (53.05%). PPI therapy without any other intervention was needed by 303 pts. (40.18%) and 11 pts. (1.46%) received surgery. Coil embolization was needed in 44 pts. (5.84%).

The matched pair analysis regarding patients with re-bleeding that could not be treated by endoscopy was not able to identify one of the above-mentioned risk factors as being significant. 5 pts. (0.66%) died from peptic ulcer bleeding.

Conclusion: Our study confirms well-known risk factors for peptic ulcer bleeding and re-bleeding. However, treatment success after re-bleeding cannot be predicted by the same factors.

Disclosure: Nothing to disclose

P1132

ENDOSCOPIC RESECTION OF UPPER GASTROINTESTINAL SUBMUCOSAL TUMOURS: ESD, STER AND EFTR

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Introduction: Upper gastrointestinal submucosal tumours (U-SMTs) are infrequent but may contain malignant potential. Some may require removal for treatment and on occasion definitive diagnosis may necessitate complete U-SMT excision. A range of techniques have been developed to facilitate endoscopic removal and avoid surgical resection, even for lesions involving the muscularis propria (MP). This includes endoscopic submucosal dissection (ESD), submucosal tunnelling endoscopic resection (STER) and endoscopic full-thickness resection (EFTR).

Aims & Methods: We conducted a prospective observational study over 84 months until October 2019 (NCT 02306707). Procedure technique was guided by pre-resection endoscopic appearance, cross-sectional imaging and predicted MP involvement based on endoscopic ultrasound (EUS). For each lesion, all resection techniques were available. Large oesophageal lesions were planned for STER and gastric lesions for ESD or EFTR with endoscopic suture closure. Lesions >30mm were consented for possible laparoscopic gastrotomy for specimen retrieval by the surgical team.

Results: 59 endoscopic resections for U-SMTs were performed (mean age 61 ± 12, 57.6% male). Procedures included ESD (n=47, 79.7%), STER (n=7, 11.9%) and EFTR (n=5, 8.5%; Table 1). Mean lesion size was 22±14 mm. Pathology included leiomyoma (29.3%), neuroendocrine tumours (27.6%), GISTs (12.1%) and granular cell tumours (10.3%). 45 (76.3%) patients were admitted for observation, with median length of stay of 1 day (IQR 1-2). There were no adverse events.

Technical success for ESD was 87.2%. En bloc resection was achieved in 97.6%. Involvement of the MP was identified in 7 (14.9%) cases and did not correlate with tissue layer on EUS (p=0.83). Six lesions were deemed non-resectable intra-procedurally and were referred to surgery, with five located in the stomach (p=0.15). Two lesions resected by EFTR, of 40mm & 50mm size, required laparoscopic gastrotomy for retrieval.

	ESD (n=47)	STER (n=7)	EFTR (n=5)	Total (n=59)
Mean size (±SD)	19 ± 13mm	30 ± 10mm	39 ± 9 mm	22 ± 14mm
Oesophagus	15/47 (31.9%)	7/7 (100%)	0/5 (0%)	22/59 (37.2%)
Duodenum	6/47 (12.8%)	0/7 (0%)	0/5 (0%)	6/59 (10.2%)
Stomach	26/47 (55.3%)	0/7 (0%)	5/5 (100%)	31/59 (52.5%)
MP involvement	7/47 (14.9%)	7/7 (100%)	5/5 (100%)	19/59 (32.2%)
Admission for observation	33/47 (70.2%)	7/7 (100%)	5/5 (100%)	45/59 (76.3%)
Technical success	41/47 (87.2%)	7/7 (100%)	4/5 (80.0%)	52/59 (88.1%)
En-bloc resection	40/41 (97.6%)	7/7 (100%)	4/4 (100%)	51/52 (98.1%)
Length of Stay (median)	1 (IQR 1-1)	1 (IQR 1-4)	6 (IQR 2-6)	1 (IQR 1-2)

[Table 1: Clinical & lesion outcomes of upper gastrointestinal submucosal tumour endoscopic resection]

Conclusion: U-SMTs can be effectively treated with endoscopic resection techniques. As the extent of MP involvement may not be reliably appreciated by EUS or cross-sectional imaging, a switch between endoscopic resection approaches should be considered intra-procedurally if required.

Planned resection for lesions >30mm should involve a surgical team for consideration of laparoscopic gastrotomy to retrieve the specimen, as this still allows for organ preservation.

Disclosure: Nothing to disclose

P1133 WITHDRAWN

P1134

AN ARTIFICIAL INTELLIGENCE BASED SYSTEM NAMED INTELLIGENT DETECTION ENDOSCOPIC ASSISTANT (IDEA), IMPROVES ESOPHAGOGASTRODUODENOSCOPY WITHOUT BLIND SPOTS IN REAL-TIME

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Introduction: Observing the whole stomach during esophagogastroduodenoscopy (EGD) is a basic prerequisite for the diagnosis of upper gastrointestinal lesions. However, supervision of EGD quality is difficult and lacks of effective tools. The aim of this study was to design an artificial intelligence (AI)-assisted EGD system to automatically record operation time and monitor blind spots in real-time.

Aims & Methods: The combination of deep convolutional neural network (DCNN) and long short-term memory (LSTM) is used for IDEA. A total of 170297 images and 5779 endoscopic videos were collected to train the system. All the images and videos were labelled by experienced endoscopists. Then we evaluate the performance of IDEA in recognition of gastric sites as well as recording EGD operation time in images and in videos respectively. Primary outcome measures included diagnostic accuracy, sensitivity and specificity.

Results: To evaluate the performance of DCNN in recognition of gastric sites in images, 3100 EGD images were collected as testing group. The sensitivity, specificity and accuracy of DCNN were 97.18%, 99.91% and 99.83% respectively. To evaluate the performance of IDEA for recognition of gastric sites in EGD videos, 129 videos were used as testing group. The sensitivity, specificity and accuracy of IDEA were 96.29%, 93.32% and 95.30% respectively. IDEA correctly record the operation time in 99.22% (128/129) videos.

Conclusion: IDEA achieved high accuracy for recognition of gastric sites and record operation time in real-time. It could be a powerful assistant tool for monitoring on blind spots and improving the quality of endoscopy.

Disclosure: Nothing to disclose

P1135

POST OESOPHAGEAL ENDOSCOPIC SUBMUCOSAL DISSECTION STRICTURES - IS RISK RELATED TO PATHOLOGY? A EUROPEAN COMPARISON OF BARRETT'S VERSUS SQUAMOUS NEOPLASIA

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Introduction: Endoscopic submucosal dissection (ESD) is a minimally invasive therapeutic option for early oesophageal neoplasia, however is not without risk. In Europe, the complication profile is most established for Barrett's neoplasia, being the predominant pathology, and stricture risk has been shown to be related to lesion circumference.

Aims & Methods: Our aim was to compare the safety of ESD between Barrett's and squamous neoplasia in a Western population. This was a retrospective analysis of all oesophageal ESDs performed within 3 tertiary referral centres in Europe. The primary outcome was post procedure stricture rate.

Results: 226 oesophageal ESDs from 201 patients were included, consisting of 167 Barrett's and 59 squamous neoplasia. Average age was 70.7 in Barrett's and 68.5 in squamous neoplasia, lesion size 34.6mm and 34.2mm and en bloc resection rate 96.6% and 94.6% respectively. The complication rate was 3/167 perforations or delayed bleeds and 7/167 strictures in Barrett's, with 1/58 perforations or delayed bleeds and 15/58 strictures in squamous (1 patient lost to follow up). Circumferential lesion involvement did increase stricture risk, but did not account for the difference between the two groups (table 1).

Lesion circumference (%)	Strictures in Barrett's ESD (n, %)	Strictures in Squamous ESD (n, %)	p-value
≤1/3	0/98 (0.0%)	3/23 (13.0%)	<0.001
>1/3-2/3	1/56 (1.8%)	6/26 (23.1%)	0.001
>2/3	6/13 (46.2%)	6/9 (66.7%)	0.354

[Table 1 - Stricture Risk Stratified by Circumferential Lesion Involvement]

Conclusion: ESD remains a low risk therapeutic option for early oesophageal neoplasia, however the stricture risk is higher in squamous neoplasia, irrespective of circumferential lesion involvement. We would suggest counselling patients with squamous neoplasia for a higher risk of stricture and having a lower threshold for steroid injection or prophylactic dilatation in these patients.

Disclosure: Nothing to disclose

P1136

TWO-SIDED SPONGE (TSS) TREATMENT- A MODIFIED ENDOSCOPIC VACUUM TECHNIQUE FOR ANASTOMOTIC LEAKS AND PERFORATIONS IN THE UPPER GASTROINTESTINAL TRACT AND SMALL BOWEL

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Introduction: Endoscopic vacuum therapy (EVT) is a highly effective treatment of anastomotic leaks and perforations in the gastrointestinal tract. However, due to its size and elasticity, reaching and precise application of the sponge into lesions distal the esophagus or above the rectum is challenging. In 2014, a modified technique for EVT has been proposed. For "two-sided sponge" (TSS) treatment, the sponge system is connected to a percutaneous abdominal drain. [1]. Subsequently, the sponge can be moved independently of the endoscope by pulling either the abdominal drain or the oral drain.

Aims & Methods: In this retrospective study, we report on 30 consecutive cases treated with TSS due to leaks and perforations in the upper GI tract and small bowel at our institution between 2012 and 2020. Primary endpoints were healing of the lesion and avoidance of revisional surgery, secondary endpoints were procedure-related complications, technical procedural data (e.g. number of sponge exchanges), length of hospital stay and in-hospital mortality.

Results: Mean age was 57 (±15) years. Indication for TSS was anastomotic leakage in 63% of cases (19/30), and acute perforation in 37% of cases (11/30). The lesions were located in the esophagus in 20% (6/30), stomach 43% (13/30), duodenum 20% (6/30) and jejunum 17% (5/30) respectively. Placement of TSS was successful in all cases. Sponges were exchanged after 4-5 days, a median of 4 sessions were necessary (range 2-20). Median length of stay was 70 days (range 34-136). Successful healing of the lesion with TSS alone was achieved in 70% of cases (21/30). In 3 cases a residual leak after TSS was successfully treated by temporary stent placement. Taken together, revisional surgery could be avoided in 80% of cases. There was one minor and no major complication. In-hospital mortality was 17% with no procedure-related death. Follow-up was a median of 249 days (range 6-2634).

Conclusion: Two-sided sponge therapy is a safe and effective method for treatment of leaks and perforations at difficult anatomic locations in the upper GI-tract and the small bowel. Revisional surgery can be avoided in the majority of cases.

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Disclosure: Nothing to disclose

P1137

ARTIFICIAL INTELLIGENCE IN DETECTING ESOPHAGEAL SQUAMOUS CELL CARCINOMA BY ENDOSCOPIC ULTRASOUND

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Introduction: Esophageal squamous cell carcinoma (ESCC) is commonly diagnosed by endoscopic ultrasound (EUS). Submucosal saline injection (SSI) during EUS examination was reported to improved the diagnostic accuracy of T1 ESCC sub-staging, while there still 6% of the patients are misdiagnosed. Artificial intelligence (AI), as a promising accessorial technology, has already been applied in endoscopy, but its application in EUS is limited.

Aims & Methods: We aim to explore the efficiency of the AI diagnostic system developed using deep learning algorithms in detecting ESCC by EUS. We initiated a diagnostic study at a single hospital. The EUS images (with/without SSI process) from consecutive ESCC patients were randomly assigned into the training and the validation datasets with a ratio of 8:2. The training dataset was used to develop the AI diagnostic system, and diagnostic performance of which was evaluated with the validation datasets.

Results: From January 2019 to June 2019, 249 patients with ESCC (206 males, age 61.1±8.23 years) were enrolled, including 152 cases of T1 stage, 31 cases of T2 stage, 31 cases of T3 stage, and 35 cases of T4 stage. A total of 2829 EUS images (93 images with SSI process from T1 stage) were collected. The diagnostic accuracy of the AI system in detecting ESCC was 80.1% [95%CI 0.772-0.830]. The AI system achieved a superior diagnostic accuracy in identifying T34 ESCC than T12 stage (80.5% [95%CI 0.760-0.850] versus 71.4% [95%CI 0.661-0.749]; $P=0.038$). Combined with SSI, the AI system achieved a superior diagnostic accuracy than those without SSI process in identifying T1 ESCC (86.3% [95%CI 0.810-0.916] versus 74.6% [95%CI 0.597-0.895]; $P<0.05$).

Conclusion: AI achieved high diagnostic accuracy in detecting ESCC, with superior diagnostic accuracy in identifying advanced ESCC. While combined with SSI, AI shown promising performance in identifying T1 ESCC.

Disclosure: Nothing to disclose

P1138

ENDOSCOPIC SURVEILLANCE IN CARRIERS OF A PATHOGENIC VARIANTS IN *CDH1* OR *CTNNA1*

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Introduction: Pathogenic germline variants in *CDH1* or *CTNNA1* are associated with a high risk for diffuse gastric cancer (DGC) and in case of *CDH1* for lobular breast cancer (LBC). Carriers of a pathogenic variant often show

multiple foci of signet ring cell carcinoma (SRCC) at early age and are advised to undergo prophylactic total gastrectomy (PTG). Multigene panel tests have identified increasing numbers of carriers of pathogenic variants in *CDH1* or *CTNNA1* who lack a family history of DGC. We evaluated outcomes of endoscopic surveillance for carriers of pathogenic variants of *CDH1* or *CTNNA1* with and without family history of DGC.

Aims & Methods: Individuals from 22 families with pathogenic germline variants of *CDH1* or *CTNNA1* were evaluated at the National Center for Hereditary Tumor Syndromes Bonn, Germany from 2008 through April 2020. Outcomes of esophagogastroduodenoscopy examinations, histopathology analyses, and surgeries were compared between individuals with and without a family history of DGC.

Results: We identified 45 carriers of a pathogenic germline *CDH1* variant and 2 carriers of a pathogenic germline *CTNNA1* variant (18 male/ 29 female). In carriers of a pathogenic *CDH1* variant LBC was diagnosed in 7/29 female patients. A history of other malignancies was apparent in 2/45 *CDH1* carriers (colorectal cancer at age 30; astrocytoma at age 29).

All patients underwent endoscopic examinations. In 15/47 patients (age range 14-53) DGC was detected during endoscopy by either targeted (9 patients) or multiple random biopsies (6 patients; number of biopsies taken 30-57). Three female patients presented with metastatic disease (16, 33 and 34 years), one patient (19 years) with positive endoscopy refuses surgery at present.

The remaining 11 patients (age range 14-53) underwent therapeutic gastrectomy, revealing additional SRCC foci in 4/11 patients (36%; number of cancer foci 1-6).

Twenty-six of the 32 patients without endoscopic detection of SRCC agreed to undergo PTG. Here, a SRCC was detected in 19/26 (73%) patients, including multifocal SRCCs in 13/19 patients (number of cancer foci 1-15). All SRCCs were confined to the mucosa (T1a).

Excluding the six patients that denied PTG, 34/41 (83%) patients were diagnosed with diffuse gastric cancer. Endoscopy yielded false negative results in 19/34 (56%) Excluding 4 patients with biopsy proven cancer without surgery, in 22/30 patients (73 %) cancer foci were missed by endoscopy.

Cancer foci were located in the cardia (6 patients with total number of 8 cancer foci), fundus (14 patients with 30 foci), body (18 patients with 38 foci) and antral region (7 patients with 11 foci).

12/34 subjects with SRCC had no diagnosis of DGC in first-degree relatives and 10 patients (29%) did not meet established criteria for *CDH1* or *CTNNA1* analysis based on a 3-generation family pedigree.

Conclusion: In 83 % of the individuals with pathogenic germline variants of *CDH1* or *CTNNA1* had histopathologic evidence of DGC in endoscopy and/or gastrectomy. Family history of DGC and endoscopic findings were no reliable determinants of risk of SRCC in individuals with genetic predisposition to DGC. Based on these findings PTG should be offered to all patients with a pathogenic germline variant in *CDH1* or *CTNNA1*.

Disclosure: Nothing to disclose

P1139

Z - POEM AS A TREATMENT OPTION FOR ZENKER'S DIVERTICULUM: OUR EXPERIENCE AT A TERTIARY CARE CENTRE IN INDIA

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Introduction: Zenker's diverticulum (ZD) is a sac-like outpouching of the mucosa and submucosa through Killian's triangle. ZD is actually a "false" diverticulum or a pseudodiverticulum.

Treatment options include open surgery or transoral rigid or flexible endoscopy and are aimed at eliminating the functional outflow obstruction and restore continuity at the pharyngoesophageal junction through septotomy with or without resection of the diverticulum.

Aims & Methods: Aim: To evaluate efficacy and safety of Z-POEM (Submucosal Tunneling Endoscopic Myotomy) for Zenker's Diverticulum.

Methods: This is a retrospective study at a single tertiary care centre in India . The Z- POEM technique was performed using principles of submucosal tunneling endoscopy with prior experience from POEM technique for achalasia cardia.

All procedures were done under general anaesthesia with endotracheal intubation. Patients were placed in the supine or left lateral position depending on the septum coming vertical. A high definition standard flexible upper gastrointestinal endoscope (GIF-HQ 190, Olympus) fitted with a clear cap was used in all patients. The flexible endoscope was carefully advanced across the narrow and thin hypopharynx and into the esophagus. The entire esophagus was examined. After the initial examination, a thorough cleaning of the diverticulum was performed, if required using sterile 0.9% saline. Intravenous antibiotics were administered to all the patients as per protocol. Carbon dioxide (CO₂) on low flow setting was used during all procedures.

A mucosal bleb is created 1-2 cm proximal to the septum using 5-10 mL of a mixed solution of 1% indigo carmine, normal saline and diluted epinephrine. A 1.5-cm mucosal incision is performed along the long axis of the septum with a triangular tip endoscopic submucosal dissection (ESD) knife. The submucosal space is entered with the aid of the cap. Submucosal tunneling is performed in the direction of the septum using a triangular tip knife.

Once the septum is reached, tunneling is extended on both sides of the septum, facilitated by repeated injection of blue-dyed saline to bulk the submucosal space. At the completion of the tunneling, the septum is exposed. Then, an ESD knife with insulated tip is used to perform the septotomy. Septotomy is extended to the base of the septum until the longitudinal muscle fibers of the esophagus proper are exposed, delineating the completion of septum dissection. Complete hemostasis is achieved. The mucosotomy is securely closed using through-the-scope(TTS) clips.

Results: Sixteen patients (Male 62.5%, Mean age 73.2 ± 5.2 years) were included with a mean Charlson comorbidity index of 4.32 . The mean size of ZD was 34.8 ± 10.0 mm. The technical success rate was 100%. Clinical success was achieved in 100% (16/16) with a decrease in mean dysphagia score from 2.9 to 0.2 ($p < 0.0001$). The mean procedure time was 47 ± 7.9 minutes, mean length of septotomy was 31.9 ± 9.4 mm and the mean length of hospital stay was 1.2 ± 0.4 days.

Adverse events were observed in 31.25% (5/16). Two patients had pain, two patients had capnomediastinum, and one patient had intraprocedural bleed. All were managed conservatively. At the 18-month follow-up, 2(12.5%) patients reported dysphagia recurrence, but did not require repeat intervention.

Conclusion: Endoscopic management of ZD using the POEM technique is a promising new technique with improved efficacy and safety. However, long-term follow-up is needed to ensure the durability of response.

Disclosure: Nothing to disclose

P1140 WITHDRAWN

P1141

THE FEASIBILITY STUDY OF PARTIAL SUBMUCOSAL INJECTION TECHNIQUE COMBINING UNDERWATER EMR FOR SUPERFICIAL DUODENAL EPITHELIAL TUMORS

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Introduction: The strategy of superficial duodenal tumor (SDET) has been controversial. Endoscopic mucosal resection (EMR) for SDET is generally difficult to capture the lesion with endoscopic snare because submucosal injection quickly spread bloody. A notable problem of underwater EMR (UEMR) for SDET is that en bloc resection rate is relatively low because floated part of lesion usually disturbs visualization of distal edge of lesion. To overcome these problems, we decided to inject only partially into the anal side of the lesion in combination with UEMR (PI-UEMR).

Aims & Methods: The aim of this study is to evaluate clinical feasibility and safety of PI-UEMR for SDET. This is a prospective observational study from tertiary care hospital. We performed PI-UEMR in patients with SDET that is 13-20mm in diameter, or less than 13mm with technical difficulty for EMR and UEMR from January 2019 to March 2020. PI-UEMR was performed as below; At first, we filled the lumen of duodenum with warmed normal saline after evacuating air. Then we promptly injected sodium hyaluronate with a small amount of indigo carmine into submucosal layer in proper part of the lesion. After that we captured the lesion with recognizing sufficient margin with endoscopic snare. Finally, we resected the lesion with electro current. After resection, we check residual lesion and if the lesion remained, we perform additional resection with same snare. Finally, we closed the wound with endoscopic clip. Primary outcome was en bloc resection rate that was defined as resection without remnant lesion endoscopically. Secondary outcomes were R0 resection rate, mean total procedure time, and intra-/post- procedure complication. R0 resection was defined as en bloc resection with free vertical and horizontal margin in histopathological examination. Procedure time was defined as the time from submucosal injection to closure of the resected wound. Complications were defined as bleeding or perforation which were necessary additional intervention.

Results: Thirty patients were included in this study. Mean age was 62±12 years old. Three fourths lesions were located at anal side from major papilla. Median lesion size was 12mm [IQR 10-16mm]. Twenty-four cases were taken endoscopic biopsy in prior hospital and observed biopsy scar. En bloc resection rate was 97%. Ro resection rate was 83%. Mean total procedure time was 17±12minutes. And there was an only one case of complication; intra-procedure bleeding that was controllable with hemostatic forceps.

Conclusion: PI-UEMR could enable to one of an endoscopic treatment technique for duodenal lesion even including relatively large lesion because of safety and usability in this study.

Disclosure: Nothing to disclose

P1143

LONG-TERM CLINICAL OUTCOME OF PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA INVADING INTO THE MUSCULARIS MUCOSAE WITHOUT LYMPHOVASCULAR INVASION AFTER ENDOSCOPIC RESECTION

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Introduction: Endoscopic resection (ER) is a standard treatment for patients with superficial esophageal squamous cell carcinoma (ESCC). After ER, additional esophagectomy or chemoradiotherapy (CRT) is recommended, when the tumor invading the muscularis mucosae (MM) with lymphovascular invasion (LVI) was revealed with pathological evaluation, because it was reported that the risk of lymph node metastasis was higher than cases without LVI. Recently, the Japan Gastroenterological Endoscopy Society (JGES) published clinical guidelines of ER for ESCC, and they released the non-negligible incidence (5.6%) of lymph node recurrence after ER for patients of pMM without LVI according to the results of systemic review[1]. However, it is not determined that those findings in previous reports were analyzed using reliable data of precise pathological evaluation using immunohistochemistry (IHC) or mature follow up period after ER.

Aims & Methods: The aim of this study was to clarify the long-term clinical outcome of patients diagnosed as ESCC invading pathologically (p) MM without LVI evaluated by Elastica van Gieson staining (EVG) and IHC using D2-40 after ER. This was a retrospective cohort study at National Cancer Hospital East using patient's medical records. Between January 2009 and December 2017, the consecutive patients who underwent ER for ESCC and who met the following criteria were included in this study: (1) tumor invasion of the MM, (2) negative for vertical margin, (3) negative for lymphovascular invasion evaluated by EVG and D2-40, (4) duration of follow-up longer than 12 months, (5) no additional treatment after ER, (6) no other primary invasive cancer with stage II-IV within 5 years before ER. We evaluated the cumulative recurrence rate (CRR), cause-specific survival (CSS), and overall survival (OS) after ER. This study was approved by the ethics committee in our institution.

Results: Totally, 67 patients were enrolled in this study. The patients were 61 men and 6 women with a median age of 67 years. The tumor location of esophagus was cervical/ upper thoracic/middle thoracic /lower thoracic in 1/9/35/22 patients, respectively. Endoscopic submucosal dissection and endoscopic mucosal resection were performed in 57 and 10 patients, respectively. The median pathological tumor size was 25 mm (range 3-164 mm). During the median follow-up time of 60 months (range 12-117 months), three patients (4.5 %) had lymph node and/or distant recurrence. Two patients developed locoregional lymph node recurrence at 16 and 43 months after the ER. The other developed multiple lymph node and bone metastases at 52 months after the ER.

Though all three patients were treated with systemic chemotherapy or CRT for recurrence, all had died of the primary esophageal cancer. The 3-/5-year CRR, CSS and OS were 1.5%/6.5%, 100%/97.4% and 100%/92.7%, respectively.

Conclusion: The risk of lymph node or distant recurrence after ER alone for patients of pMM ESCC without LVI was similar to previous reports even when using precise histological evaluation using IHC with mature follow-up period. Further investigation using larger population is needed to verify the necessity for additional treatment after ER for this cohort.

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Disclosure: Nothing to disclose

P1144

SIMULATION OF DIFFERENT UPPER GASTROINTESTINAL BLEEDING TYPES FOR PRACTICING HEMOSTASIS IN FLEXIBLE ENDOSCOPY

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Introduction: Gastrointestinal bleeding is the most frequent cause of emergency endoscopy. Life threatening complications might arise, depending on the etiology and intensity of the hemorrhage. Endoscopic diagnostics and simultaneous therapy are the first line treatment of upper gastrointestinal bleeding. Practicing emergency situations is essential but actually no adequate and realistic option for training exists so far.

Aims & Methods: Aim of this project is the development of a training model with modular exchangeable bleeding sources, followed by a multicenter evaluation by endoscopists of each skill level. The model is completely free of animal material. The artificial organs consist of latex and silicone and are equipped with artificial vessels for bleeding simulation and can be attached to a bleeding pump. Via 3D printing, exchangeable modules for fast integration of the bleeding sources are created. An artificial mucosa is prepared according to a novel protocol.

Results: Multiple types of bleeding sources (reflux esophagitis, esophageal varices, gastric and duodenal ulcer) can be implemented into a model for esophagogastroduodenoscopy. The following therapeutic interventions are conductible: variceal banding, stent application, injection, clipping, thermal processes and application of topical substances for hemostasis. Four centers agreed to conduct an evaluation of this training model. Due to the COVID-19 pandemic, the evaluation could not be performed yet, but will be completed until the UEG week.

Conclusion: Our training model enables practicing endoscopic diagnostics and therapy of upper gastrointestinal bleeding and offers a combination of realistic conditions and a broad spectrum of interventions.

Disclosure: Nothing to disclose

P1145

WATER PRESSURE METHOD AND NEEDLE-TYPE ENERGY DEVICE WITH WATER JET FUNCTION IMPROVES OUTCOMES OF DUODENAL ESD

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Introduction: Duodenal endoscopic submucosal dissection (ESD) is considered technically challenging with a high risk of adverse events. However, recently, we have made some progress in the ESD technique and device by introducing two features: the water pressure (WP) method and the second-generation ESD knife (DualKnife™) with water jet function (DualKnife J™).

Aims & Methods: The present study aimed to assess whether this recent progress improved the clinical outcomes of duodenal ESD. This was a retrospective observational study. Of patients who underwent ESD for superficial duodenal epithelial tumors (SDET) from June 2010 to December 2018, patients in whom a single expert performed the procedure were included in this study. Various factors, including the WP method and ESD devices (DualKnife™ or DualKnife J™), and treatment era (early, mid, and late) were analyzed to determine whether they were associated with intraprocedural perforation and procedure time. The treatment era was defined by dividing the study period equally among 3 subgroups according to the period of the treatment.

Results: The procedure time was significantly shortened, and the proportion of intraprocedural perforations was the lowest in the late phase. Multivariate analysis of the usage of the WP method revealed a significant decrease in the intraprocedural perforation rate (OR, 1.04; 95% CI, 1.01-1.06), and analysis of the usage of both the WP method (β coefficient -0.40, P value < 0.01) and DualKnife J™ (β coefficient -0.10, P value 0.032) revealed an independent negative correlation with procedure time.

Conclusion: In conclusion, the present study revealed that the WP method significantly reduced the intraprocedural perforation rate and that both the WP method and DualKnife J™ significantly shortened the procedure time of duodenal ESD.

Disclosure: Nothing to disclose

P1146

LONG TERM OUTCOMES AND PROGNOSTIC FACTORS OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER IN PATIENTS AGED ≥ 75 YEARS

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Introduction: Elderly patients with early gastric cancer (EGC) who meet the indication of endoscopic submucosal dissection (ESD) has been increasing. However, there is controversy to decide the treatment strategy for elderly patients with EGC. We aimed to evaluate the clinical outcomes and prognostic factors for overall survival (OS) of elderly patients who underwent ESD for EGC.

Aims & Methods: Between January 2006 and December 2018, 439 patients aged ≥ 75 years who had undergone ESD for EGC at Severance Hospital were analyzed. The clinical outcomes and prognosis were evaluated. Independent risk factors for OS were identified in elderly patients who underwent ESD for EGC.

Results: Mean age of the study population (302 men; 137 women) was 78.3 (range 75-92 years) years. Heavy alcoholics and patients who have smoking history were 36 (8.2%) and 219 (49.9%), respectively. The most frequent comorbidity was hypertension (n=255, 58.1%), followed by diabetes mellitus (n=101, 23.0%). The median Onodera prognostic nutritional index (PNI) was 50.1 (range 35.0-115.0), and the neutrophil to lymphocyte ratio (NLR) was 3.2 (range 0.5-36.0). En bloc, R0, and curative resections were achieved in 96.8% (n=425), 90.7% (n=398), and 75.6% (n=332), respectively, without severe complications. During the follow-up period (median 54.2 months, range 4.0-159.6 months), 86 patients died, including 3 of gastric cancer. The 3-, 5-, and 10-year OS were 91.2%, 83.5% and 54.5%, respectively.

In multivariate analysis, smoker (HR=3.96; 95% CI, 2.05-7.65; $P < 0.001$), cancer history of the other organs (HR=1.78; 95% CI, 1.30-4.52; $P = 0.006$), NLR > 1.6 (HR=1.83; 95% CI, 1.04-3.21; $P = 0.035$), Charson comorbidity index (CCI) ≥ 3 (HR=1.83; 95% CI, 1.32-3.20; $P = 0.001$), presence of lymphovascular involvement (LVI) (HR=2.63; 95% CI, 1.21-5.73; $P = 0.015$) were the independent risk factor for poor OS.

Conclusion: The long term outcome of ESD for elderly patients with comorbidities was poor than for those without. Thus, these prognostic factors can be used to decide the therapeutic approach for EGC in elderly patients, including the necessity of additive surgery after ESD of EGC and a close follow-up.

Disclosure: Nothing to disclose

P1147

GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) BY A TRAINEE IS A RISK FACTOR FOR POST-ESD ELECTROCOAGULATION SYNDROME

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Introduction: Gastric endoscopic submucosal dissection (ESD) has recently been markedly improved as a less invasive treatment for early gastric cancer. Post-ESD electrocoagulation syndrome (PECS), one of the complications after gastric ESD, is a clinically important condition, possibly leading to delayed perforation. As risk factors for PECS, sex (female), prolonged treatment, specimen and tumor sizes, and piecemeal resection have been reported.

However, these risk factors implicate the need for strict postoperative management in almost all cases, and it has been necessary to establish preoperative risk factors. Therefore, our aim was to clarify risk factors for PECS after gastric ESD, and establish satisfactory postoperative management.

Aims & Methods: A retrospective cohort study was conducted involving 264 patients who underwent gastric ESD for stomach cancer at our hospital between April 2011 and December 2014. The practitioners were divided according to their experience into expert (> 50 cases) and trainee (< 50 cases) groups. The primary endpoints were comorbidities, operative time, maximum tumor size, and complications (secondary hemorrhage, perforation, and PECS with fever $> 37.0^{\circ}\text{C}$ and abdominal pain within 4 days after ESD).

Results: After excluding 56 patients with two or more lesions resected simultaneously during ESD or with positive margins by microscopic pathological diagnosis, 208 patients, including 154 males (74.0%), with a mean age of 73 years (range, 42-90 years) were examined. The expert and trainee groups included 79 and 129 patients, respectively. Both groups had no significant difference in sex, comorbidities, or maximum tumor size.

Significantly higher values ($p < 0.001$) in the trainee group for operative time (40 vs. 50 minutes in the expert and trainee groups, respectively) and the incidence of PECS (11.4 vs. 22.6% in the expert and trainee groups, respectively) were found by univariate analysis. Multivariate analysis also demonstrated significantly higher values in the trainee group for operative time (odds ratio 1.01, 95% CI 1.00-1.02, $p = 0.026$) and the incidence of PECS (odds ratio 2.430, 95% CI 1.07-5.51, $p = 0.034$).

Conclusion: Gastric ESD is difficult and requires skill; therefore, a longer operative time is needed for trainees, resulting in the increased incidence of PECS. As most institutions specify their protocols regarding the duration of hospitalization for gastric ESD, risk factors for PECS should be predicted before ESD. ESD by a trainee is a predictable risk factor, although prolonged operative time, specimen and tumor sizes, and piecemeal resection can be evaluated only after ESD. Therefore, for gastric ESD by a trainee, postoperative management in consideration of the onset of PECS is necessary.

Disclosure: Nothing to disclose

P1148

SNARE-TIP SOFT COAGULATION IS EFFECTIVE AND EFFICIENT AS A FIRST-LINE MODALITY FOR TREATING INTRAPROCEDURAL BLEEDING DURING BARRETT'S MUCOSECTOMY

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Introduction: Intraprocedural bleeding (IPB) during multi-band mucosectomy (MBM) for Barrett's neoplasia (BN) can obscure the endoscopic field. Current hemostatic devices require disassembly of the mucosectomy apparatus, affecting procedure continuity and technical success. Snare-tip soft coagulation (STSC) is an evidence-based modality in the colorectum but has not been studied in this setting. We aimed to evaluate the efficacy of STSC for IPB during MBM.

Aims & Methods: Between January 2014 and November 2019, 191 patients underwent MBM for BN within a prospective, observational cohort in two tertiary centers. Standard MBM technique was performed. IPB was defined as bleeding obscuring the endoscopic field that required intervention. STSC and other standard hemostatic techniques were used to treat IPB.

The primary outcome was the technical success of STSC. Secondary outcomes were risk factors for IPB, technical success by rescue hemostatic modalities, need for disassembly of the mucosectomy apparatus and safety.

Results: 292 MBM procedures were performed in 191 patients. IPB occurred in 63 procedures (21.6%; 95% CI 17.3 - 26.7%). In 51 IPBs, STSC was used as the first-line modality with hemostasis being achieved in 48 (94.1%; 95% CI 84.1 - 98.0%). In patients with major (pulsatile) IPB treated with STSC, 75% achieved hemostasis. There were no adverse events related to STSC. One episode of delayed bleeding (2.0%; 95% CI 0.4 - 10.3%) occurred after STSC, which was successfully treated by repeat endoscopic intervention.

Conclusion: Snare-tip soft coagulation is a safe, effective and efficient first-line hemostatic modality for minor and major IPB during MBM for BN.

Disclosure: Nothing to disclose

P1149 WITHDRAWN

P1150

MULTISPECTRAL ENDOSCOPY FOR EARLY DETECTION OF DYSPLASIA IN BARRETT'S OESOPHAGUS: A FIRST-IN-HUMAN PILOT STUDY

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Introduction: Barrett's oesophagus (BO) is an acquired condition that predisposes patients to the development of oesophageal adenocarcinoma through intermediate stages of dysplasia. Early detection of dysplasia allows curative endoscopic therapy, but the current diagnostic standard of care based on random biopsies, has low sensitivity as dysplasia is often inconspicuous on white light endoscopy. Multispectral imaging (MSI) allows simultaneous collection of morphological (spatial) and biochemical (spectral) information from tissue, which we hypothesised could help to more effectively delineate disease.

Aims & Methods: To test our hypothesis, we constructed a clinically translatable multispectral endoscope using an imaging fibre bundle (PolyScope) that can be introduced through the accessory channel of a standard gastroscope to collect spectral information *in vivo*. The device includes both a spectrometer, to capture high spectral resolution information from a single point, and a spectrally resolved detector array (SRDA), to capture spatially-resolved spectral information across 9 spectral filters.

Patients referred for endoscopic surveillance of BO or endoscopic treatment of BO-related neoplasia were enrolled in a pilot clinical study (NCT03388047). MSI was performed by introducing the multispectral endoscope through a 3.7mm working channel of a therapeutic gastroscope. In each patient, two regions of interest, one with inconspicuous BO and one with a suspicious lesion, if present, were selected for MSI. These were marked, to allow coregistration of imaging and subsequent biopsies, then interrogated using the multispectral endoscope. Biopsy or endoscopic resection were performed to provide histopathological diagnosis.

Results: Coregistration of histopathology and multispectral imaging was possible in 15 patients at 28 distinct tissue regions, 18 of which had evidence of non-dysplastic BO and 10 of dysplasia or early cancer. White light and multispectral endoscopy recordings were synchronised and multispectral image frames containing the marked tissue region of interest were selected for further analysis, resulting in 653 frames labelled with pathology (486 non-dysplastic and 167 dysplastic). These frames were processed to yield tissue absorption spectra, which demonstrate conserved differences in absorption between different disease classes across multiple patients.

Distinct haemoglobin absorption is apparent at ~540 and ~570 nm. By fitting the absorption spectra of oxyhaemoglobin and deoxyhaemoglobin to the acquired spectra, we were able to extract measures of oxygen saturation, blood volume fraction and vessel radius from the tissue. These showed significant differences between tissue classes ($p < 0.05$) indicative of aberrant neovascularisation early in the progression of disease.

Conclusion: The results of this pilot study indicate that a spectral contrast exists between dysplastic and non-dysplastic regions, which can be used for diagnostic purpose. With future development of miniaturised SRDAs fitted on the endoscope tip and neural networks for classification, MSI has the potential to provide high contrast for BO-related neoplasia during endoscopic surveillance.

Disclosure: Nothing to disclose

P1151

USE OF ENDOSCOPE TIP CONTROL SIMULATOR TO PREDICT THE CLINICAL SKILLS TO PERFORM ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)

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Introduction: Measurement of the quality of endoscopy is essential but can be complex, time-consuming and costly. The measurement can be simplified if we can establish the relationship between simulation-based assessment of skills and the quality of care delivered. In addition, a simulation-based assessment may be useful to identify deficiencies in the required skills and, in turn, to develop strategies designed to improve these skills efficiently. Delicate endoscope tip deflection movements are critical in performing ESD. We hypothesize that the endoscope tip deflection simulator can be useful to provide predictors of the ability to perform ESD.

Aims & Methods: We invited endoscopists who have at least one year of gastric ESD to participate in this study. We used a validated tip deflection simulator¹⁾ to measure their ability to control the endoscope tip. In brief, the endoscopists used the left hands to control the tip of the endoscope and move the tip from “A” to “Z.” We measured the “Bowl Simulator Time (BST)” as the time required to complete the task and averaged the best three measurements. We defined “slow” BST as ≥ 50 seconds and “fast” BST as < 50 seconds. We then obtained of previously recorded data of their ESD time (ESDT), which is the time to complete the resection of intramucosal lesions measuring ≤ 20 mm, without ulceration or scar and stratified the data according to the experience and location of the lesion (antrum vs. corpus). We defined beginner endoscopists when they have performed ≤ 100 cases and experienced > 100 cases. We used Pearson correlation coefficient to explore the correlations between BST and ESDT.

Results: A total of 36 endoscopists (92% male, age 36 ± 4 years) from 5 institutions across Japan participated in the study. 21/36 have performed less than 100 ESD cases (median 30 [range: 5-80]) and 15/36 have performed more than 100 cases (median 140 [range: 100-500]) (Table).

BST was significantly correlated to the ESDT for the resection of lesions in the corpus among beginner endoscopists: ESDT in fast and slow BST groups was 45 ± 16 min vs. 73 ± 20 min ($p=0.008$). In these resections, ESDT was linearly correlated: $R^2=0.50$ [95%CI: 0.03-0.79, $p=0.041$]. These correlations were not observed among the experienced endoscopists. The average BST was 53 ± 14 sec (range 33-103, median 49.5): BST was not cor-

related to the number of experienced ESD: $R^2=-0.02$ [95%CI -0.35-0.31, $p=0.897$. Beginner endoscopists with good tip deflection control (low BST) were as good as experienced endoscopists for resection of lesions in the corpus.

Characteristics	
N	36
Median age [range]	36 [29-46]
Gender (M:F)	33:3
Experience in ESD (Median [range])	75 [5-500]
Bowl Simulator Results (Mean $\pm$ SD, Median [Range])	53 $\pm$ 14, 49 [33-103]

[Characteristics of participants]

Conclusion: Simulation-based assessments of endoscope tip deflection skills can be useful to identify the efficient beginning gastric ESD performers. In turn, mastery of tip deflection using the simulators may facilitate the development of skills to perform ESD.

Dr. Uedo and Dr. Soetikno contributed equally to this study conduction.

References: 1) Surg Endosc. 2017;31(12):5364-5371. doi:10.1007/s00464-017-5617-7

Disclosure: Nothing to disclose

P1152

DIFFERENCES IN CLINICAL FACTORS ASSOCIATED WITH TECHNICAL DIFFICULTY BETWEEN CONVENTIONAL AND TRACTION-ASSOCIATED ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ESOPHAGEAL CANCER

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Introduction: Conventional endoscopic submucosal dissection (ESD) for esophageal squamous cell carcinoma (ESCC) is technically difficult and requires long procedure times. Recently, the superiority of traction assisted (TA) using clip with thread ESD to conventional esophageal ESD in procedure time was confirmed in the randomized controlled trial. However, which clinical factors have improved or remained in terms of technical difficulty after introducing the TA esophageal ESD remains unclear.

Aims & Methods: We aimed to investigate the differences in clinical factors associated with technical difficulty between conventional and TA ESD. Herein, we enrolled consecutive naïve ESCC patients treated with ESD in our hospital from April 2010 to June 2014 as the conventional cohort and from January 2016 to December 2019 as the TA cohort. Lesions at the cervical esophagus were excluded. We used a hemoclip and thread equipment in TA ESD. Technically difficult cases, which were defined as ESD requiring ≥ 120 min, perforation development during procedure, and/or piecemeal resection, were extracted from both cohorts. And clinical factors associated with technical difficulty in each cohort were evaluated and compared. If the baseline characteristics between the two cohorts differed, additional subgroup analysis was performed.

Results: Totally, 276 lesions in 265 patients in the conventional cohort and 421 lesions in 387 patients in the TA cohort were enrolled. The median length of the lesion was 32 mm in the conventional cohort and 29 mm in the TA cohort. The proportion of lesions with circumference $\geq 1/2$ of the lumen in the conventional cohort (42%) was greater than that in the TA cohort (26%), while other characteristics were similar. The number of

technically difficult cases and median procedure time in the conventional cohort and TA cohort were 85 (29%) and 71 (17%) lesions, and 80 and 60 min. Multivariate analysis in the conventional cohort showed that the lesion length (mm) as the continuous variable (odds ratio (OR) 1.05, 95% CI 1.02-1.08), tumor location at lower esophagus (vs. upper/middle, OR 1.47, 95% CI 1.18-1.85), lesion circumference $\geq 1/2$ (vs. $< 1/2$, OR 2.41, 95% CI 1.65-3.51), and predominant wall on the left (vs. anterior/posterior/right, OR 1.65, 95% CI 1.14-2.39) were independent factors associated with technical difficulty, in the TA cohort revealed that the lesion length (mm) as the continuous variable (OR 1.10, 95% CI 1.07-1.13), tumor location at lower esophagus (vs. upper/middle, OR 1.90, 95% CI 1.30-2.77), lesion circumference $\geq 1/2$ (vs. $< 1/2$, OR 3.58, 95% CI 1.55-8.29).

Subgroup analysis as to the lesion circumference showed that the proportion of technically difficult cases with circumference $< 1/2$ and $\geq 1/2$ were 11% and 57% in the conventional cohort, 5% and 49% in the TA cohort. Regarding the lesion located on the left wall, which is associated with technical difficulty in conventional cohort, the proportion of technically difficult cases with circumference $< 1/2$ and $\geq 1/2$ were 14% and 83% in the conventional cohort and 3% and 57% in the TA cohort, respectively.

Conclusion: While the proportion of technically difficult cases with TA ESD is lower than that with conventional ESD, the independent clinical factors of technical difficulty are common in both methods. (the lesion length, tumor location at lower esophagus, and lesion circumference $\geq 1/2$ of the lumen) except for the left wall. As for lesion on the left wall, the proportion of technically difficult cases were reduced with TA ESD, compared to conventional ESD.

Disclosure: Nothing to disclose

P1153

EFFICACY OF ENDOSCOPIC PREVENTION OF DELAYED ADVERSE EVENTS AFTER ENDOSCOPIC RESECTION OF THE DUODENUM: A META-ANALYSIS

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Introduction: Although various procedures have been used to prevent serious adverse events after endoscopic resection of the duodenum, their effectiveness has not been determined. In this study, we conducted a systematic review and meta-analysis to determine whether endoscopic preventive procedures reduce delayed adverse events.

Aims & Methods: Studies regarding endoscopic treatment for superficial nonampullary duodenal tumors (SNADETs) were selected. We compared the following two groups: the closure group, which underwent mucosal sutures and coverage of mucosal defects after resection, and the unclosed

group, which did not. The primary outcome was the rate of delayed adverse events, including perforation and bleeding. The pooled risk ratios (RRs) of all investigated outcomes, the 95% confidence intervals (CIs) and P-values were calculated.

Results: Four studies were included in the meta-analysis. The pooled overall adverse event rates in the closure group and unclosed group were 3.6% and 21.1%, respectively. This rate was significantly lower in the closure group (RR 0.19, 95% CI: 0.10-0.38, $P < 0.01$, $I^2 = 0\%$), and the rate of delayed bleeding was significantly lower in the closure group (RR 0.14, 95% CI: 0.06-0.33, $P < 0.01$, $I^2 = 0\%$). Regarding delayed perforation, the RR in the closure group was 0.39 (95% CI: 0.12-1.32, $P = 0.13$, $I^2 = 0\%$).

Conclusion: Preventive procedures significantly reduced the risk of delayed adverse events by more than 80%. After endoscopic resection of the duodenum, the implementation of preventive procedures, including mucosal sutures and coverage of mucosal defects, to delay adverse events is strongly recommended.

Disclosure: Nothing to disclose

P1154

LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR UNDIFFERENTIATED EARLY GASTRIC CANCER, BEYOND EXPANDED CRITERIA

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Introduction: Expanded indication of endoscopic submucosal dissection (ESD) for intramucosal undifferentiated early gastric cancer (EGC) up to 2 cm without lymphovascular invasion have been accepted. Without Intramucosal undifferentiated early gastric cancer (EGC) up to 2cm in size without ulceration has been treated by endoscopic submucosal dissection (ESD) because the incidence of lymph node metastasis negligible.

Aims & Methods: . The aim of this retrospective study was to analyze the long-term outcomes of ESD carried out to treat undifferentiated EGC in two groups (group A: up to 2 cm, group B: 2-3 cm). Between January 2001 and March 2015, 104 patients with undifferentiated early gastric cancer (EGC) including poorly differentiated adenocarcinoma (PD, n=66) or signet ring cell carcinoma (SG, n=38) on preoperative biopsy underwent ESD (group A: 71cases, group B: 33cases) , Total ESD specimens were evaluated en bloc resection, R0 resection, and curative resection (CR) and to evaluate long term outcome, annual endoscopic surveillance with biopsy and CT scan were done.

Results: M/F was 40/31 and 17/16.

Mean follow up period in group A and B were 61.10 $\pm$ 38.12, 60.79 $\pm$ 47.75.

Mean age in group A and B were 52.90 $\pm$ 13.62, 57.00 $\pm$ 12.25

En bloc in group A and B were achieved in 92.9%, 90.9% of patients, respectively (NS).

R0 resection in were achieved in 87.3%, 51.5% of patients, respectively ($p < 0.05$).

Curative resection was 83.0 % in group A and group B was not include this definition.

Postoperative bleeding, perforation during the procedure, and delayed perforation were no significantly different in both groups, respectively.

Recurrence in group A and B were 5.6% (n=4), 18.1% (n=6), retrospectively ($p < 0.01$). All cases with lateral margin positive required additional ESD (n=2), desctructive therapy (n=3), or surgery (n=4) and no recurrence happened.

No patient died of gastric cancer.

Conclusion: In group B, R0 resection rate was lower than group A but R0 resection in both group were not different recurrence rate with long term follow up. Carefully, undifferentiated EGC with 2 to 3 cm in a size recommended ESD.

Disclosure: Nothing to disclose

P1155

DEEP NEURAL NETWORK FOR THE DETECTION OF EARLY NEOPLASIA IN BARRETT'S OESOPHAGUS

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Introduction: Missed oesophageal adenocarcinoma occurs within one year of index endoscopy in a quarter of patients undergoing surveillance for Barrett's oesophagus (BE). Increased efforts are necessary to improve early neoplasia detection in BE so that early curative endotherapy can be offered. Computer aided diagnosis can support endoscopists to improve detection. The aim of this study was to develop a deep neural network that can aid in the diagnosis of early neoplasia in BE.

Aims & Methods: Videos were prospectively collected in high definition white light and i-scan Pentax (Hoya, Japan) imaging modes in patients with dysplastic lesions in BE (high grade dysplasia/intramucosal adenocarcinoma) and patients with non-dysplastic Barrett's oesophagus (NDBE). The combination of endoscopic resection margins/targeted biopsy sites and histology served as the ground truth for areas of dysplasia in the videos. All videos with segments of dysplasia were annotated for definite presence of dysplasia. We trained a convolutional neural network with a Resnet101 architecture to classify images into dysplastic or non-dysplastic using randomly selected frames from annotated videos. The classifier was evaluated on high quality images selected for expert annotation (Dysplastic and non-dysplastic). The expert endoscopist delineations on these images served as the ground truth.

Results: A total of 123 different patients each with a video of BE assessment (68 with HGD/Intramucosal cancer and 55 controls (53 NDBE, 2 normal oesophagus) were included in the study. The cases were randomly divided into three independent groups: training (N = 68, 34 dysplasia, 34 controls), validation (N = 11, 6 dysplasia, 5 controls) and testing set (N = 44, 28 dysplasia, 16 controls). For training, a balanced dataset was created with equal numbers of dysplastic and non-dysplastic frames. All available dysplastic frames were used whereas non-dysplastic frames from the oesophagus were chosen randomly. The neural network was trained using a total of 148,936 frames. This was then tested on 86 iscan-1 images from 28 dysplastic BE patients, and 47 iscan-1 and white light images from 16 non dysplastic BE patients.

The neural network classified dysplasia in BE with a sensitivity of 95%, specificity of 83% and accuracy of 91% in the testing set. The area under the ROC was 0.97 (Table 1).

Heat maps generated from the classifier algorithm overlapped with the expert ground truth delineation in 98% (80/82) of the test set images where a true positive classification of dysplasia was made. Using an overlap threshold of at least 20%, heat map outputs for 76% (62/82) of all the testing set images had a Dice score greater than the threshold.

Testing data set	
Accuracy	91%
Sensitivity	95%
Specificity	83%
Delineation outcome	98% (80/82)

[Table 1: Performance outcome of the AI system]

Conclusion: Preliminary data suggest that a convolutional neural network can be trained to detect dysplastic BE mucosa with accuracies similar to expert endoscopists. The algorithm was created from annotations using whole videos which minimised selection bias. Heat maps generated from the classifier model was able to identify areas of dysplasia in the majority of cases. This can potentially aid as a screening tool during BE surveillance endoscopy allowing for targeted biopsies and minimise the need for Seattle protocol biopsies which would save on costs, procedure time and provide additional time for other procedures.

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P1156 WITHDRAWN

P1157 WITHDRAWN

P1158

WILL RANDOM 100 PROCEDURES BE ENOUGH TO ESTIMATE UPPER GASTROINTESTINAL ENDOSCOPY QUALITY METRICS?

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Introduction: Assessing the quality in upper gastrointestinal endoscopy by performance measures is a major priority of gastrointestinal endoscopy units. However, the practicality and feasibility of the implementation of the assessment is an issue. The European Society of Gastrointestinal Endoscopy (ESGE) suggests the possibility of the evaluation of 100 procedures to estimate upper gastrointestinal endoscopy quality metrics in a cohort instead of a complete evaluation of the all cohort.

Aims & Methods: We intended to evaluate if performance measures of 100 random procedures can be representative of all other procedures. We performed a retrospective cohort study including all upper gastrointestinal endoscopies performed in a single centre between 2016 and 2019. We compared performance measures defined by ESGE of all procedures vs. 100 random procedures. Automatic generated sample using SPSS. Statistical analysis with Qui² test.

Results: We evaluated 3866 procedures. Comparing the cohort vs. 100 sample: there was not a significant difference between the two groups for key performance measures: proper instructions for fasting (99.8% vs. 100%; p=0.93); procedure time registration (98% vs. 97%; p=0.79); accurate photodocumentation (66% vs. 58%; p=0.14); standardized terminology application (40% vs. 23%; p=0.09); registration of complications after therapeutic procedures (immediate complications: 77% vs. 100%; p=0.12;

delayed complications: 81% vs. 78%; $p=0.81$). Seattle biopsy protocol application in Barrett's esophagus surveillance was not evaluated because of the small number of cases. For minor performance measures, there were not significant differences in inspection time in the stomach (74.3% vs. 73.8%; $p=0.90$) nor in biopsy protocol according to MAPS guidelines (69% vs. 79%; $p=0.25$). The small number of cases did not allow evaluation of inspection time in Barrett's esophagus, Lugol staining in the esophagus for patients at risk of squamous cell carcinoma and Barrett's esophagus patients entered a registry to monitor the incidence of dysplasia.

Conclusion: In our cohort, the use of just 100 sample of procedures offers enough accuracy to infer the quality metrics of the full upper gastrointestinal endoscopy cohort and might be used as a resource solution in cases where the full cohort cannot be assessed, simplifying the audit process.

Disclosure: Nothing to disclose

P1159

BILE ACID SEQUESTRANTS IN NON-HEALING BARRETT'S ESOPHAGUS AFTER ENDOSCOPIC THERAPY - A RETROSPECTIVE EVALUATION

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Introduction: Endoscopic resection of the mucosal adenocarcinoma of the esophagus and its dysplastic precursors, followed by ablation of the remaining Barrett's esophagus (BE), can be considered as an accepted standard. To ensure sufficient secondary prophylaxis, healing of the BE with squamous epithelium is necessary. The therapy in the absence of healing has not been systematically investigated and remains unclear. At our centre, a therapy trial with bile acid sequestrants is carried out in cases of insufficient squamous re-epithelialization under maximum PPI therapy (3 x40 mg PPI/d).

Aims & Methods: Retrospective analysis of the neoplasia of the gastro-esophageal junction treated in a center with inadequate squamous healing from April 2014 to March 2020. All cases with ICD-10 key C15.9 are extracted from the clinical software. These are systematically examined for indications of a wound healing disorder.

Results: In 1157 patients 76 with documented wound healing disorder can be extracted. The mean age of the predominantly male patients (92.1%) was 65.5 years.

In the resection phase, 26 patients (34.2%) under maximum PPI therapy showed partial healing. In 35 patients (46.1%) no reepithelialization could be observed. When the therapy was extended by bile acid sequestrants ($n=52$), 54.2% ($n=26$) healed and 16.7% ($n=8$) partially healed. No improvement was observed in 29.2% ($n=14$).

With intensified therapy, healing was achieved in 50.0% ($n=21$) and partial squamous epithelial healing in 28.9% during ablation ($n=52$). In 21.1% no healing could be achieved.

In 31 patients (40.7%) surgery became necessary during the course of therapy. Of these, 19 patients (25%) received a fundoplication and 11 patients (14.5%) an esophageal resection.

Conclusion: Supplementing acid suppression with PPI with bile acid sequestrants should be attempted before surgery if there is no re-epithelialization.

Disclosure: Nothing to disclose

P1160

CHALLENGING DETECTION OF MINUTE GASTRIC CANCERS USING IMAGE-ENHANCED ENDOSCOPY WITH ARTIFICIAL INTELLIGENCE

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Introduction: Image recognition by artificial intelligence (AI) has currently exceeded human capability, and actual adoption of AI-assisted endoscopy in clinical practice is promising. However, in the adoption of AI to surveillance esophagogastroduodenoscopy (EGD), further discussion to improve the detection of minute gastric cancers (GCs) with less than 5 mm in major diameter is inevitable. It is sometimes difficult even for experts to discover hard-to-find GCs (e.g., minute GCs and GCs after eradication) against background of chronic gastritis.

Therefore, detection rates for smaller GCs were known to exhibit enormous disparity among endoscopists, since screening EGD is performed by wide ranges of clinicians, from inexperienced trainees to skillful experts. To address such variations among endoscopists, we have developed an AI application to EGD focused on GC detection, and reported that our AI system using deep learning through convolutional neural networks produces an excellent sensitivity for GC detection of 92.2% (71/77 lesions) in total, but 16.7% (1/6 lesions) for minute GCs. [Ref.1] It was annotated that this research had some limitations for image inclusion criteria: learning image datasets of our AI algorithm included images with image-enhanced endoscopy (IEE) such as narrow band imaging (NBI) and indigo-carmin dye contrast (IC) method, though high-quality white light images (WLIs) were only comprised as image datasets for verification.

Aims & Methods: To verify and resolve the issue that current AI approaches are likely incompatible with reliably detecting minute GCs by only WLIs, the following study was planned.

In 17,527 screening EGDs performed by 11 endoscopists between 2017 and 2018 at New Tokyo Hospital, early 123 GCs including 31 minute GCs were histologically diagnosed by endoscopic resection. The detection rate for early GCs and minute GCs were 0.72% (range 0.17~2.63) and 0.18% (range 0.00~0.89), respectively.

We selected five patients, in which minute GCs laboriously found by the highest detector, to compare the efficacy of detection by AI algorithm with and without IEE procedure. Prior AI algorithm, the expert could detect only one of five lesions by WLI screening, and the other four lesions were eventually encountered by IEE using NBI or with IC method. The associated images from the five screening EGDs combined with IEE were validated by our AI systems.

Results: AI failed to detect all of these GCs in only WLIs, and 3 out of five (60%) were detectable by AI with IEE. The three lesions were detectable at least in one non-magnifying IEE view despite using multiple GC-centralized and GC-focused images. AI was able to recognize a minute GC after HP eradication, which the expert eventually detected as light-brownish areas in surrounding greenish area by non-magnifying NBI view.

Moreover, AI system was also able to detect a flat type of GCs of which subtle depression was enhanced by IC methods. On the other hand, characteristics of AI-undetectable two lesions indicated a macroscopic type with depressed irregular-shaped erosions that were barely discoverable by WLIs in retrospective inspection.

Conclusion: A new AI method using IEE in addition to WLIs should effectively identify minute GCs.

References: 1) Hirasawa T, Aoyama K, Tanimoto T, et al. Application of artificial intelligence using a convolutional neural network for detecting gastric cancer in endoscopic images. *Gastric Cancer* 2018;2:653-60.

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P1161

CLINICAL OUTCOMES AND ADVERSE EVENTS OF THE STOMACH ENDOSCOPIC SUBMUCOSAL DISSECTION OF THE MID TO UPPER STOMACH UNDER GENERAL ANESTHESIA AND MONITORED ANESTHETIC CARE

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Introduction: Endoscopic submucosal dissection (ESD) of gastric tumors in the mid to upper stomach is a technically challenging procedure. This study compared the therapeutic outcomes and adverse events following ESD of tumors in this area, performed in conjunction with either general anesthesia (GA) or monitored anesthetic care (MAC).

Aims & Methods: Between 2012 and 2018, 674 patients underwent ESD of gastric tumors in the midbody, high body, fundus, or cardia (100 patients received GA; 574 received MAC). The results were analyzed using propensity score (PS)-matched (1:1) patients receiving either GA or MAC.

Results: PS matching identified 95 patients who received GA and 95 matched patients who received MAC. Both groups showed high rates of en-bloc resection (GA, 98.5%; MAC, 98.9%; $p = 0.18$) and complete resection, defined as tumors excised with histologically confirmed negative margins (GA, 82.1%; MAC, 90.5%; $p = 0.14$). There were no significant differences in the frequencies of adverse events (GA, 16.8%; MAC, 9.5%; $p = 0.13$) between the anesthetic groups. A logistic regression analysis indicated that the anesthetic method was not a factor impacting the frequencies of complete resection or adverse events.

Conclusion: At our high-volume center, good therapeutic outcomes were achieved following ESD of tumors in the mid to upper stomach, regardless of the anesthetic method used. Our results demonstrate the efficacy and safety non-inferiority of the ESD procedure performed in conjunction with MAC, compared with GA.

Disclosure: Nothing to disclose

P1162

UPPER GASTROINTESTINAL ENDOSCOPIC FINDINGS IN DYSPEPTIC PATIENTS WITHOUT ALARM SYMPTOMS

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Introduction: Dyspepsia is a common condition which is frequently encountered in clinical practice. Dyspepsia is not associated with a high risk of malignancy, but patients are often concerned that malignancy is the cause of their symptoms. Current guidelines for the management of dyspepsia recommend only an endoscopy in patients older than 60 years or with alarm symptoms. Despite this, endoscopy is often performed in patients with dyspepsia younger than 60 years and without alarm symptoms.

Aims & Methods: This study aims to evaluate upper gastrointestinal findings in dyspeptic patients without alarm symptoms. This retrospective study was conducted with data from a multicenter database with anonymously collected structured endoscopy reports. Patient characteristics and endoscopy outcomes were automatically extracted from these endoscopy reports and stored in the database. For this study, all upper GI endoscopies performed in patients with dyspepsia as indication between 2015 and 2019 were analyzed. Patients with alarm symptoms such as dysphagia, odynophagia, gastrointestinal bleeding, unintentional weight loss, anaemia, persistent vomiting, palpable epigastric mass or family history of upper gastrointestinal cancer were excluded.

The primary outcome was a major endoscopic finding defined as the presence of an ulcer, stricture or suspicion of neoplasia found during upper GI endoscopy. Secondary outcomes were a minor endoscopic finding, defined as presence of esophagitis or suspicion of Barrett's esophagus or gastric metaplasia, and the yield of repeat endoscopies with dyspepsia as an indication.

Results: During the five year period, 27,908 upper GI endoscopies with dyspepsia as the indication for the investigation were recorded, performed in 26,440 patients. After excluding patients with alarm symptoms, a total of 23,796 patients were included. (median age 56.0 years, range: 18 - 96 years, 37.3% male). A major endoscopic finding was found in 603 patients (2.5%): a gastric ulcer in 204 patients (0.9%), duodenal ulcer in 177 patients (0.7%), esophageal stricture in 55 patients (0.2%) and duodenal stricture in 12 patients (0.1%). Suspicion of neoplasia was noted in 171 patients (0.7%), including 80 patients (0.3%) with suspicion of esophageal neoplasia, 88 patients (0.4%) with suspicion of gastric neoplasia and 11 patients (0.05%) with suspicion of duodenal neoplasia. Esophagitis was recorded in 3651 patients (15.3%), suspicion of Barrett's esophagus in 877 patients (3.7%) and suspicion of gastric metaplasia in 975 patients (4.1%).

A total of 998 patients (4.19%) underwent more than one endoscopy with dyspepsia as indication and during one of the subsequent investigations a new diagnosis was recorded in 19 patients (1.9%) including suspicion of neoplasia in 2 patients (0.2%).

Conclusion: In patients with dyspepsia without alarm symptoms major findings are found in 2.5% of patients. A lesion suspicious for esophageal, gastric or duodenal neoplasia was noted in 0.7% of cases. For patients

undergoing repeat endoscopies for dyspepsia this was even lower (0,2%). This study provides further proof that upper GI endoscopy in patients presenting with dyspepsia without alarm symptoms, apart from patients' reassurance, is unlikely to be cost-effective.

Disclosure: Nothing to disclose

P1163

ALMAGATE SUSPENSION SPARING TO TREAT THE ENDOSCOPIC SUBMUCOSAL DISSECTION-INDUCED GASTRIC ULCERS: A SINGLE-CENTER RANDOMIZED STUDY

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Introduction: Endoscopic submucosal dissection (ESD) has been widely used as an first-line therapy to surgical resection for patients with early gastric cancer (EGC). However, large artificial ulcers are developed after ESD procedures, which results in a higher risk of perforation and delayed bleeding.

Aims & Methods: To evaluate the efficacy and safety of magnesium aluminum suspension spraying in the treatment of gastric ulcer after ESD surgery. A prospective analysis of patients with gastric ESD surgery between January 2016 and June 2019. They were divided into the control group, spraying group and spraying + oral group on the basis of treatment methods. All patients were followed 8 weeks to evaluate endoscopic ulcer healing and recovery rate. At the same time, the postoperative symptoms and complications such as bleeding were also recorded. SPSS 24.0 software was used for statistical analysis.

Results: 330 eligible cases were randomly divided into control group (124 cases), spraying group (108 cases) and spraying + oral group (98 cases). The results showed that the postoperative pain incidence of spraying group and spraying + oral group were significantly better than the incidence of control group (35.48% vs. 17.59%, $P < 0.01$; 35.48% vs. 20.41%, $P = 0.01$). The 4-week ulcer recovery rate of spraying + oral group was better than the rate of control group. It should be noted that ulcer healing rate achieved 100% for antrum of patients in spraying + oral group. At the same time, the incidence of postoperative bleeding decreased, and no significant adverse drug reactions were observed during the follow-up.

Conclusion: Almagate suspension spraying is safe and effective in the treatment of upper gastrointestinal ESD postoperative ulcer, which can also relieve the postoperative pain.

Disclosure: Nothing to disclose

P1164 WITHDRAWN

P1165

MANAGEMENT OF STRICTURES AFTER ENDOSCOPIC RESECTION FOR EARLY ESOPHAGEAL NEOPLASIA

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Introduction: Endoscopic resection of extensive esophageal neoplastic lesions is associated with a high rate of esophageal stricture. Most studies have focused on the risk factors for post-endoscopic esophageal stricture, and data from Western centers are scarce.

Our aim is to describe the management of esophageal strictures following endoscopic submucosal dissection (ESD) or mucosal resection (EMR) for early esophageal neoplasia.

Aims & Methods: We included consecutive patients treated by endoscopic resection for early esophageal neoplasia followed by endoscopic dilatation at a tertiary referral center. The demographic, endoscopic, histological characteristics, and stricture treatment outcome were.

Results: Between January 2010 and December 2019, 166 EMR and 261 ESD were performed for early esophageal neoplasia, and 34 (8.0%) patients developed an esophageal stricture requiring endoscopic treatment. The indication for endoscopic resection was Barrett's neoplasia in 15/34 (44.1%) cases and squamous cell neoplasia in 19/34 (55.9%) cases. The median (IQR) number of endoscopic dilatations was 3.6 (2-4). 26.5 % (9/34) patients only requested 1 dilatation, and 65% had a complete relief after 3 sessions. The median number of dilatations was significantly higher for SCN (4.5 (2-6); range 1-17; $p=0.03$), and in case of circumferential resection (5.1 (3-7); $p=0.03$). Endoscopic dilatation allowed a sustained dysphagia relief in 33/34 (97.0%) patients after a mean follow-up of 25.8 $\pm$ 22 months.

Conclusion: Refractory post-endoscopic esophageal stricture is rare. After a median of 3.6 endoscopic dilatations, 97.0% of patients were permanently relieved of dysphagia Circumferential endoscopic esophageal resections should be considered when indicated.

Disclosure: Nothing to disclose

P1166

ENDOSCOPIC PAPILLECTOMY FOR EARLY AMPULLARY TUMORS: OUTCOMES FROM A LARGE MULTICENTER OBSERVATIONAL STUDY

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Introduction: Endoscopic papillectomy (EP) has been reported to be an efficient treatment for ampullomas and early ampullary carcinomas (T1a). While it has lower morbidity and mortality rates than surgery, it also exposes the patient to severe complications such as pancreatitis, severe bleeding or duodenal perforation. However, data are scarce regarding its morbidity and long term efficacy in routine practice.

Aims & Methods: The aims of our study were to evaluate the efficacy and safety of EP and to determine risk factors for recurrence and complications in a large cohort of patients.

This is a retrospective multicenter observational study. All patients who underwent EP in 5 tertiary referral centers between January 2008 and December 2018 were included. Morphological and histological characteristics of lesions, modalities of EP, complications and endoscopic follow-up were collected. Success rate was defined as the absence of tumoral residue on the last follow-up endoscopy. Risk factors for recurrence and complication were analyzed using univariate and multivariable Cox regression with 95% confidence intervals.

Results: 227 patients were included (sex ratio 1.1, mean age 61 years). Mean tumors size was 20 mm. Regarding final histology, 48% of tumor had low grade dysplasia (n = 108), 33.3% high grade dysplasia (n = 75) and 10.7% invasive adenocarcinoma (n = 24). Pre-therapeutic assessment revealed duodenal extension in 23.9 % of cases and intraductal invasion in 15.5% of cases. The resection was *en bloc* in 65.2% cases and R0 in 45.2% cases. The median follow-up was 22.3 months. The recurrence rate was 32% (n = 64) with a median time to recurrence of 6.8 months. 60.7 % of recurrences were treated efficiently by additional endoscopic treatment.

Finally, success rate reached 82.8% (n = 173).

In multivariate analysis, incomplete resection (OR : 2.50, 95%IC : 1.23-5.09, p=0.011), intraductal invasion (OR :2.55, 95%IC :1.11-5.86, p=0.028) and tumor size >2cm (OR : 2.06, 95%IC : 1.06-4.01, p=0.034) were significantly correlated with endoscopic recurrence.

Complications included pancreatitis (17.6%), bleeding (11%), perforation (5.2%) and biliary stenosis (2.6%). The mortality was 0.9%. Prophylactic pancreatic stent placement significantly decrease significantly the risk of post procedural pancreatitis (OR : 0.41, p <0.014). Tumor size >2 cm was significantly associated with bleeding (OR : 3.31, p<0.006).

Conclusion: Results of this large multicenter retrospective study confirm that EP is an efficient and relatively safe endoscopic treatment. It also suggests that R1 resection, intraductal invasion and lesion size > 2 cm are significantly correlated with endoscopic recurrence, which can be efficiently treated by additional endoscopic interventions in approximately 2/3 of cases.

Disclosure: Nothing to disclose

P1167

TECHNICAL AND CLINICAL SUCCESS OF ENDOSCOPIC FISTULAE CLOSURE: A MULTICENTER COLLABORATIVE STUDY

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Introduction: New endoscopic techniques such as gastrointestinal (GI) stenting, full thickness suturing, and over the scope clips have had significant impact on the management of GI fistulae. These techniques have

shown promising results, but further information is needed on the technical and clinical success along with follow up information. The aim of this study is to analyze the technical and clinical success of endoscopic GI fistulae closure.

Aims & Methods: Patients were included from 7 centers internationally. Data was retrospectively collected for demographic features (age, gender, ethnicity, comorbidities), etiology and location of the fistulae, procedural characteristics along with outcomes (technical success, clinical success, adverse events, short term follow up information).

Technical success was defined as closure of the fistulae as reported by the endoscopist. Clinical success was defined as closure of the fistulae on follow-up.

Results: A total of 79 patients were included. Mean age was 54.6 years, 38% male. 25% patients had a malignancy diagnosis. The most common location of the GI fistulae was stomach (54.4%, n=43). The different methods employed for the management included over the scope clip (n=35), stent (n=14), full thickness suturing (n=25), and through-the-scope clips (n=15). Technical success was 87%. Overall clinical success was 84%. Persistent closure was achieved in 59% of patients after 1 procedure. 30% of patients underwent a 2 endoscopic procedure (n=20) and 11.6% (n=8) patients underwent a third procedure due to persistent/reopened fistula (41%, n=28). The same number of patients underwent surgery (11.6%, n=8). Overall complication rate across all endoscopic procedures for fistula repair management was 11.4%. Follow-up time was 3.7 months.

Conclusion: Advances in endoscopic technology and techniques have allowed gastroenterologists to close fistulae which were previously being managed surgically. Our study shows that although it make take more than 1 procedure, fistula closure is obtainable in a majority of patients. Future large sample sized studies can be used to evaluate which risk factors are predictive of clinical success for short term closure.

Disclosure: Nothing to disclose

P1168

GASTRIC PER-ORAL ENDOSCOPIC MYOTOMY VERSUS PYLOROMYOTOMY: AN INTERNATIONAL COMPARATIVE STUDY

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Introduction: Gastroparesis is a potentially debilitating gastric motility disorder with limited treatment options. Symptoms can result in hospitalization and poor nutrition requiring nutritional support. Treatment options with highest efficacy include gastric peroral endoscopic myotomy (GPOEM) and surgical pyloromyotomy. Limited information is available comparing these two techniques.

Aims & Methods: We aim to compare the efficacy and safety of GPOEM versus surgical pyloromyotomy in patients with gastroparesis. A retrospective analysis of patients who underwent GPOEM or surgical pyloromyotomy for refractory gastroparesis from 4 centers across the US and Latin America were included. Electronic medical records were used to collect data

on patient demographics, relevant imaging studies and laboratory values, technical success, clinical success, gastroparesis cardinal symptom index (GCSI), procedure time, pre- and post-op gastric emptying times, adverse events, and hospital length of stay (LOS).

Results: A total of 102 patients were included (mean age 47; 32.4% male): GPOEM n=39, surgical pyloromyotomy n=63. Age and pre-op BMI were not statistically different between the two groups (p=0.232, p=0.059, respectively). Patient demographics are outlined in Tables 1 and 2. Technical success rate was 100% in both groups. Clinical success rate was 92.3% in the GPOEM group and 82.5% in the surgery group (p=0.164). The GPOEM group had a significantly higher post-op GCSI score reduction by 1.3 units (p< 0.00001), post-op retention reduction at 2 hours by 18% (p< 0.00001), post-op retention reduction at 4 hours by 25% (p< 0.00001) and a lower procedure time by 20 minutes (p< 0.00001) as compared to surgery. GPOEM also had a lower hospital LOS by 2.8 days (p< 0.00001). Adverse event rates were significantly lower in the GPOEM group (13%) compared to the surgery group (33.3%; p=0.021). Mean blood loss in the GPOEM group was only 3.6 ml as compared to 866 ml in the surgery group.

Conclusion: GPOEM may be a less invasive, safer, and more efficacious procedural treatment for refractory gastroparesis as compared to surgical pyloromyotomy.

Disclosure: Nothing to disclose

P1169

PER ORAL ENDOSCOPIC MYOTOMY FOR ZENKER'S DIVERTICULUM: A NOVEL AND SAFER TECHNIQUE OVER SEPTOTOMY?

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Introduction: Endoscopic management of Zenker's diverticuli has traditionally been via septotomy technique. The recent development of the tunneling technique has shown to be efficacious and safe in 3 space endoscopy. The aim of this study is to evaluate the tunneling technique using per oral endoscopic myotomy (Z-POEM) versus septotomy for the treatment of Zenker's Diverticulum.

Aims & Methods: Patients who underwent endoscopic management of Zenker's Diverticulum either by Z-POEM or septotomy from March 2016 until November 2019 from 5 international academic centers were included. Demographics, clinical data pre and post procedure, size of the diverticulum, procedure time, adverse events, and hospital length of stay were analyzed.

Results: A total of 42 patients (mean age 74.2 years old, 47.6% Male) were included: septotomy (n=25), Z-POEM (n=17). Pre-procedure FOIS score and Eckardt score was 4.9 and 4.1 for the septotomy group and 6.4 and 3.4 for the ZPOEM group. The median diverticulum size was larger in the ZPOEM group, ranging from 30-49mm pre intervention, versus less than 30mm in the septotomy group. Technical success was achieved in 100% of both groups. Clinical success was achieved in 90% and 88% in the septotomy vs ZPOEM groups. Procedure time was 52 minutes vs 38 minutes for septotomy vs Z-POEM (p-value 0.03). Adverse events occurred in 24%

(n=6) in septotomy group vs 0% (n=0) in the Z-POEM group. Post-procedure FOIS score and Eckhardt scores were 6.5 and 0.16 in the septotomy group, and 7 and 0.4 in the ZPOEM group. Re-intervention for ongoing symptoms was required in 2 patients in septotomy group and 1 patient in the ZPOEM group. Mean hospital length of stay was 1.4 days vs 1.6 days (p-value 0.59).

Conclusion: The Z-POEM procedure is an efficacious and safe endoscopic treatment for Zenker's Diverticuli. Z-POEM is faster, with less adverse events compared to traditional septotomy technique. Endoscopists treating Zenker's Diverticuli should familiarize themselves with this technique.

Disclosure: Nothing to disclose

P1170 WITHDRAWN

P1171

PROSPECTIVE OBSERVATIONAL STUDY ON ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC TUMORS UNDER THE CONTINUOUS ADMINISTRATION OF ANTITHROMBOTIC AGENTS

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Introduction: Endoscopic submucosal dissection (ESD) is occasionally accompanied by serious adverse events such as post-operative bleeding. Several reports showed antiplatelet agents and anticoagulants were risk factors for the post-operative bleeding, while other reports showed continuous administration of the antiplatelet agents did not have an independent significant association with bleeding. Furthermore, most reports were conducted in retrospective design. Therefore, it is controversial whether the use of antithrombotic agents is associated with post-operative bleeding. We prospectively evaluated the effects of continuous administration of antithrombotic agents on ESD for gastric tumors.

Aims & Methods: Between April 2013 and February 2019, a total of 106 patients (122 lesions) underwent gastric ESD under the continuous antithrombotic agents. Antithrombotic agents were consisted of antiplatelet agents such as aspirin, thienopyridine or cilostazol, and antithrombotic agents such as warfarin or direct oral anticoagulants. An intravenous proton pump inhibitor (PPI) (lansoprazole, 30mg, twice daily) was started on the day of ESD and changed to oral PPI (lansoprazole, 30mg, once daily) on the next day. After April 2015, vonoprazan 20mg once daily was used instead of PPI. The patients were discharged seven days after the ESD, and received follow-up endoscopy 8 weeks after the ESD. Post-operative bleeding was defined as clinically evident bleeding that required emergency endoscopic hemostasis and/or blood transfusion with a decline of more than 2 g/dL of hemoglobin. The clinical and pathological factors associated with post-operative bleeding in patients taking antithrombotic agents were analyzed.

Results: This study population included 75 men and 31 women (median age, 79.5 years). The Antiplatelet agents were taken by 78 patients (aspirin 45, thienopyridine 20, cilostazol 20), and anticagulants were administered in 31 patients (warfarin 14, apixaban 9, dabigatran 4, rivaroxaban 4). Ten patients took multiple antithrombotic agents (dual antiplatelet 7, antiplatelet and anticoagulant 3).

En-bloc resection was achieved in all patients with R0 resection rate of 98%. Median lesion size was 14mm and median procedure time was 71minutes. Post-operative bleeding occurred in 12 patients (11%), whereas no perforation occurred. Between the post-operative bleeding group

and no bleeding group, significant differences were seen in thienopyridine ($p=0.0096$) and lesion size ($p=0.019$) in univariate analysis. Multiple anti-thrombotic agents seemed to be associated with post-operative bleeding ($p=0.085$). In multivariate analysis, thienopyridine (OR 4.5, 95%CI 1.04-19.4) and lesion size (14mm or larger; OR 5.5, 95%CI 1.29-38.5) were independent risk factors for post-operative bleeding. None of the patients developed cerebrovascular disease and ischemic cardiac disease during study period.

Conclusion: Under the continuous administration of antithrombotic agents, the use of thienopyridine or large lesion size is associated with post-operative bleeding.

Disclosure: Nothing to disclose

P1172 WITHDRAWN

P1173 WITHDRAWN

P1174 WITHDRAWN

P1175

IMPROVING STANDARDS OF UPPER ENDOSCOPY FOR BARRETT'S OESOPHAGUS BY IMPLEMENTING KEY PERFORMANCE MEASURES - A QUALITY IMPROVEMENT INITIATIVE

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Introduction: Upper gastro-intestinal endoscopy is used widely in the detection, evaluation and surveillance of Barrett's oesophagus. Early detection of neoplasia is important in the assessment of Barrett's oesophagus. However, quality metrics and well-defined criteria for performing a high quality examination for Barrett's oesophagus are lacking in comparison to colonoscopy. They may be equally important in early detection of neoplasia and improving clinical outcome.

Aims & Methods: Our study aimed to assess the impact of implementing performance measures in improving quality of endoscopy in Barrett's oesophagus. This was a single tertiary centre retrospective audit in two parts. A baseline audit established existing practice followed by implementation of performance measures and further audit 8 weeks later. Key performance measures used were:

- 1) appropriate indication, consent and safety checklist for 100% of patients,
- 2) use of Prague classification for defining the Barrett's segment,
- 3) Seattle protocol biopsies and;
- 4) inspection time of 1 minute per cm.

We also recommended use of advanced imaging techniques in patients with long segment Barrett's. We documented cases of adenocarcinoma and dysplasia through a multidisciplinary process.

Results: Initially, 807 procedures were assessed over a 2-month period to identify 35 cases of confirmed Barrett's oesophagus. 11 of these were long segment and 24 were short segment disease. Implementation of performance measures was done through a 2-hour group education meeting and discussion of the audit results, written quality standards and pictorial descriptions and reminders within the endoscopy room. Eight weeks after implementation of the standards, 420 procedures were audited to identify

28 cases of Barrett's with 19 long segment and 9 short segment disease. 100% of pre-procedure metrics were met. 3 cases of high-grade dysplasia and 1 case of adenocarcinoma were identified in the first audit (11.4%) and low-grade dysplasia rate was 2%. Post implementation audit identified 1 case of adenocarcinoma and 2 cases of low-grade dysplasia (7%). Details of procedural metrics are shown in table below.

Key Performance Measure	Pre-implementation		Post Implementation	
	Long Segment	Short Segment	Long Segment	Short Segment
Prague Classification	8/11 (72.7%)	14/24 (58.3%)	19/19 (100%)	7/9 (77.8%)
Time (1 minute/ cm)	7/11 (63.6%)	24/24 (100%)	18/19 (94.7%)	9/9 (100%)
Seattle Protocol	5/11 (45.5%)	5/24 (20.8%)	16/19 (84.2%)	6/9 (66.7%)
Advanced Imaging	8/11 (72.7%)	14/24 (58.3%)	17/19 (89.5%)	6/9 (66.7%)

[Table. Quality Metrics in Barrett's.]

Conclusion: Quality metrics are equally important in upper endoscopy especially for pre-malignant conditions such as Barrett's oesophagus. Our process of an audit followed by multiple methods of education and implementation of key performance measures was successful in our endoscopy unit. It significantly improved the use of advanced imaging, Prague criteria and adequate examination time. Our study suggests that implementation of key quality markers and performance measures improves the quality of assessment of Barrett's oesophagus.

Disclosure: Nothing to disclose

P1176

LONG-TERM RESPONSE RATE OF ENDOSCOPIC MUCOSAL RESECTION (EMR) AS A TREATMENT OF SUPERFICIAL OESOPHAGEAL NEOPLASIA IN A SPANISH REFERRAL CENTER

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Introduction: Endoscopic Mucosal Resection (EMR) is the technique that makes it possible to establish a certain diagnosis of superficial oesophageal neoplasia and, on many occasions, makes it possible to treat it. The long-term efficacy of this therapy is not well known.

Aims & Methods: The aim of this work is to establish the long-term efficacy of EMR for nodular lesions and for superficial neoplasms of the oesophagus. We present a group of 23 accumulated cases from 2009 to 2012 of patients diagnosed with High-Grade Dysplasia (HGD) (6), Adenocarcinoma (ADC) (15) or Epidermoid Oesophageal Carcinoma (2) in which EMR is performed. Seven patients (T2, 5 cases of T1b and 1 case of Epidermoid with multiple disseminated HGD foci) are referred to surgery given the therapeutic limitation of endoscopic procedures. In the 16 patients who are candidates for endoscopic treatment, EMR shows: intramucosal ADC (T1a) in 9 cases, HGD in 6 cases and Epidermoid Carcinoma (T1a with free edges) in 1.

Results: In all 16 patients, EMR was performed within the Barrett Oesophagus treatment protocol for resection of focal lesions. In 4 patients, the first EMR was performed after previous treatment with Radiofrequency Ablation (RFA) of de novo nodular lesions.

From the total of 16 patients, 13 have obtained complete eradication of intestinal metaplasia (CEIM), in 2 the histological diagnosis of ADC has persisted in subsequent controls, and in 1 intestinal metaplasia (IM) has been detected in the last control. The median follow-up time for these patients is 73 months (6 years), with an interquartile range of 33.5-86.5 months.

From the patients who obtained the CEIM, 9 have required associating other therapeutic procedures (EMR and/or RFA): 6 have required subsequent treatment with RFA, 2 with new sessions of EMR and 1 has required the combination of both (2 sessions of EMR and 3 of RFA). In total, 22 EMRs have been performed.

Conclusion: CEIM is obtained in 81% of the total of patients with a correct diagnosis of superficial endoscopic neoplasia treated with EMR, with or without the need for subsequent treatments. This is the largest spanish series with adequate results regarding the efficacy rate of this endoscopic therapy over 8 years.

Disclosure: Nothing to disclose

P1177 WITHDRAWN

P1178

DEVELOPMENT OF CONFOCAL ENDOMICROSCOPY CRITERIA FOR EARLY SIGNET-RING CELL CARCINOMA IN PATIENTS WITH HEREDITARY DIFFUSE GASTRIC CANCER SYNDROME

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Introduction: Hereditary diffuse gastric cancer (HDGC) syndrome confers a 70% lifetime risk of gastric cancer. Endoscopic surveillance with at least 30 random biopsies, at regular intervals, is recommended for individuals fulfilling HDGC criteria, who refuse or prefer to delay gastrectomy for psychosocial reasons. Signet-ring cell carcinoma (SRCC) foci can be completely inconspicuous or appear as subtle pale areas, which are generally best seen on narrow band imaging (NBI). Pale areas however are difficult to differentiate from mucosal scars from previous biopsies. The utility of probe-based confocal laser endomicroscopy (pCLE) in diagnosing SRCC foci has never been investigated. The aim of the study was to develop diagnostic pCLE criteria for early SRCC in individuals with HDGC.

Aims & Methods: This was a prospective study on patients undergoing endoscopic surveillance for HDGC. Up to 4 pale areas and one negative control region were identified by WLE and NBI, marked by diathermy coagulation (at discretion of the endoscopist) and then assessed by pCLE after intravenous fluorescein injection. Targeted biopsies were taken for histologic assessment. In the first phase of the study, two investigators assessed off-line 113 video sequences to identify pCLE features related to SRCC diagnosis. Corresponding histological diagnostic slides from the biopsies were used as a reference for pCLE. During the second phase of the study, pCLE diagnostic criteria were validated off-line in an independent video set (n = 20)

by a gastrointestinal pathologist with interest in HDGC and an endoscopist experienced in pCLE, who were blinded to the histologic diagnosis. Sensitivity, specificity, accuracy, negative and positive predictive values (NPV/PPV), and interobserver agreement were calculated.

Results: The first phase included from 50 endoscopic locations from 16 HDGC patients, Four pCLE features characteristic of SRCC were identified: (A) glands with attenuated margins, (B) glands with spiculated or irregular shapes, (C) heterogenous granular stroma with sparse glands, (D) enlarged vessels with tortuous shape and tubular flow (Figure 1). In the second phase, an independent set of video sequences (n=20) derived from 12 patients was assessed. Criteria B and C had the highest diagnostic accuracy and yielded sensitivity of 56% and 50%, respectively, and a specificity of 82% and 86%, respectively. The interobserver agreement ranged from 0.00 to 0.565. Using criteria 2 and 3 as a panel with a cut-off of one positive criterion for a diagnosis of SRCC, the panel has a sensitivity of 67% and a specificity of 83%.

No.	Criterion	Average sensitivity (%)	Average specificity (%)	Average accuracy (%)	Fleiss' kappa	Positive predictive value	Negative predictive value
1.	Glands with attenuated margins	38.8%	90.9%	67.5%	0.000	77.7%	64.5%
2.	Glands with spiculated or irregular shapes.	55.8%	81.8%	70.0%	0.565	71.4%	66.6%
3.	Heterogenous granular stroma with sparse glands.	50.0%	86.3%	70.0%	0.390	75.0%	67.8%
4.	Enlarged vessels with tortuous shape and tubular flow.	27.7%	81.8%	57.5%	0.474	55.5%	58.0%

[Performance of pCLE diagnostic criteria for HDGC in the blinded validation.]

Conclusion: We have generated and preliminarily validated pCLE criteria for early SRCC. The low sensitivity likely relates to the millimetric size of SRCC foci in most cases. Further validation and clinical reproducibility of the diagnostic criteria by multiple endoscopists is planned to be undertaken in the third phase of the study.

Disclosure: Nothing to disclose

P1179

CASE REPORT OF TRACHEOBRONCHIAL FISTULA AFTER POEM FOR CONGENITAL ACHALASIA IN A 2 YEAR OLD CHILD

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Introduction: Achalasia is an esophageal motility disorder characterized by loss of peristalsis in the distal esophagus and failure of lower esophageal sphincter relaxation. Oral endoscopic myotomy (POEM) is a new and less invasive treatment with great outcomes. Complications arising from this surgical intervention may occur, such as pneumothorax, mediastinal and subcutaneous emphysema, pneumoperitoneum. In this report we describe a case of a 2-year-old child with congenital idiopathic achalasia and grade II megaesophagus who developed tracheobronchial fistula after poem.

Aims & Methods: The POEM procedure was performed under general anesthesia with oral intubation and CO2 inflation. During the myotomy the patient developed hypertensive pneumothorax treated with puncture

drainage. Despite this, pneumothorax was re-formed and the patient had 2 cardiorespiratory arrests, reversed after CPR. The patient was then referred to the ICU, and chest drainage was performed. On the 3rd day suspected a right empyema with mediastinitis, and on the 4th day milk was seen on the drain and an upper endoscopy performed showed a tracheobronchial fistula. Antibiotics were then started and a nasogastric tube was passed with the tip covered with a gloved finger and connected to the continuous vacuum aspiration and left in the esophageal lumen for 17 days (the tube was changed on day 7).

Results: The patient evolved with progressive clinical improvement and was discharged on the 28th day after the poem.

Conclusion: Pneumothorax is a frequent complication of POEM, but tracheoesophageal fistula is not. We believe that in this case the fistula occurred due to injury during the myotomy because of the thin thickness of the esophageal muscles and proximity to the airway in children of this age. Treatment with continuous vacuum aspiration proved to be an effective option for the treatment of these fistulas.

Disclosure: Nothing to disclose

P1180

CLINICAL OUTCOMES OF NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is a standard treatment for gastric superficial lesions. Additional gastrectomy with lymph node (LN) dissection should be considered for patients with non-curative resections, owing to the risk of residual cancer (RC) and LN metastasis (LNM). Nevertheless, in clinical practice, few patients are found to have RC or LNM after additional surgery.

Aims & Methods: We aim to evaluate clinical outcomes of patients who underwent non-curative gastric ESD in our center. Patients submitted to a gastric non-curative ESD between January/2013 and October/2019 were enrolled. We analyzed local recurrence and distant metastasis during follow-up of patients not submitted to salvage surgery, and RC and LNM in patients with additional surgery.

Results: During the analyzed period 181 ESD were performed. A total of 36 resections (19,8%) were non-curative (median size 25mm [IQA 22]), from 35 patients (mean age 74.79±9.40, 22 males), and were enrolled. In 5 cases, resection was a local-risk resection (piecemeal resection n=3, positive horizontal margin=2) and surveillance was proposed; during a mean follow-up of 54 months, no recurrence was noted. The other cases (n=31) were non-curative high-risk resections. Additional surgery was performed in 14 of this patients: 2 patients had RC (both with a R1 resection) and none had LNM; 2 patients died of postoperative complications. Of the remaining 17 high-risk patients, 4 abandoned follow-up; during a mean follow-up of 25 months, neither local recurrence nor distant metastasis was found. Metachronous gastric lesion was observed in 2 patients. Among the 5 patients who died during follow-up, none died of gastric cancer.

Conclusion: In our study, over 85% of patients undergoing salvage surgery for non-curative ESD did not have RC nor LNM and 15% died of postoperative complications. None of the patients not submitted to surgery presented disease recurrence. Our results suggest that the decision of additional surgery should be individualized and careful follow-up might be an alternative in selected cases.

Disclosure: Nothing to disclose

P1181

DEFINING THE OPTIMAL TREATMENT APPROACH FOR EARLY NEOPLASIA OF THE GASTROESOPHAGEAL JUNCTION: A MULTI-CENTER RETROSPECTIVE STUDY

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Introduction: The endoscopic management of early gastroesophageal junction (GEJ) neoplasia remains unclear as there is no consensus on whether it should be classified into the esophageal or gastric category. Endoscopic resection can be challenging due to vicinity to the lower esophageal sphincter, the dense vascularization and indistinct demarcation line to subsquamous extension. The primary aim of this was to compare EMR and ESD as treatment for GEJ neoplasia.

Aims & Methods: In this retrospective multi-center cohort study we reviewed endoscopy databases at two referral centers. We identified adult patients who underwent endoscopic mucosal resection (EMR) or submucosal dissection (ESD) for early neoplasia of the GEJ. Primary GEJ neoplasia was defined as low or high-grade dysplasia (LGD/HGD) or adenocarcinoma (Ca) with the epicenter of the lesion located up to 1cm over and 2cm below the proximal margin of the gastric folds in the absence of endoscopic evidence of Barrett's esophagus. The outcomes of EMR and ESD were compared using Welch t-test and Fisher's exact test with regards to mean lesion size and the rate of curative treatment. Curative treatment was defined as complete resection (negative deep margin for piece meal resection and negative deep and lateral margin for resection *en-bloc*) (R0) of low- and high-grade dysplasia or a moderately/well differentiated Ca (G1/G2), no lymphovascular invasion (LVI-), infiltration within the superficial submucosal layer (Sm1). The initial (referral) grades were compared with the final (post-resection) lesion stages. Finally, the rates of sub-squamous extension and presence of background intestinal metaplasia (IM) within the lesions were assessed.

Results: We identified 40 patients (mean age 72.5 [±10.1] years; male: female ratio 3:1), who underwent endoscopic treatment for primary GEJ neoplasia between 2009 and 2020 (21 Warsaw / 19 Cambridge). EMR was performed for 24 lesions (60.0%) with final stages of: 3 LGD, 5 HGD, and 16 Ca (9 T1a, 6 T1b, 1 not assessed), which were removed in a median of 2 pieces (IQR: 1-3). ESD was performed for 16 lesions with final stages of: 1 LGD, 2 HGD, 13 Ca (9 T1a, 4 T1b). The mean size of lesions removed with an EMR was significantly smaller than that of lesions treated with ESD (15.9 [±10.1]mm vs 27.9 [±17.8]mm, $P=.023$). The curative, complete (R0), and *en-bloc* resection rates for EMR and ESD were 37.5% and 45.8% ($P=0.5$), 33.3% and 50.0% ($P=.001$), 75.0% and 87.5% ($P<.001$), respectively. The final diagnosis, as compared to referral diagnosis, was up-graded after endoscopic removal in 14 cases (35.0%); 3 were down-graded (7.5%). Background intestinal metaplasia was identified in just over half of cases (22/40; 55.0%). Neoplasia undermining squamous epithelium was present in 9 lesions (22.5%), of which the majority had positive resection margins (R1; 55.6%).

Conclusion: ESD showed significantly better outcomes than EMR, even for lesion smaller than 2cm, and should be regarded as the primary treatment modality for GEJ neoplasia. Squamous extension of the neoplastic epithelium is a common phenomenon, therefore broader proximal resection margins are advised.

Disclosure: Nothing to disclose

P1182

IMPROVING QUALITY OF ENDOSCOPY REPORTING USING REPORTING TEMPLATES DRIVES UP THE DETECTION OF PATHOLOGY - A TERTIARY CENTRE EXPERIENCE AT VALIDATING THE TRUE PREVALENCE OF CERVICAL INLET PATCH

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Introduction: The cervical inlet patch (CIP) is an island of heterotopic gastric mucosa, most commonly found in the proximal oesophagus. Its importance as a cause of throat symptoms has been recognised, particularly chronic globus sensation. Proton pump inhibitors are often ineffective in resolving symptoms.

Studies report variable figures regarding the presence of heterotopic gastric mucosa in the proximal oesophagus. The largest autopsy series to date (1000 cases) demonstrated a prevalence of 4.5% in children. Several studies estimated CIP prevalence at between 0.03% and 5.9%. It is likely that this variability is due to the quality of endoscopy. The identification of an inlet patch has been correlated with the awareness of the endoscopist, with one study demonstrating the detection rate falls from 2.27% to 0.29% when endoscopists studying prevalence were compared with those who were unaware.

Aims & Methods: We aimed to evaluate the true prevalence of cervical inlet patch in an enriched population of patients using quality indicators as a template to enhance detection rate.

A prospective study of presence of inlet patch documented during endoscopic BRAVO capsule procedures performed between 2009 and 2020 was undertaken. Five operators carried out the procedures with expertise in optical image enhancement endoscopy and upper -GI lesion recognition. Endoscopy reports were interrogated including picture photo-documentation to confirm presence of inlet patch. Additionally, patient symptoms and BRAVO capsule pH data were analysed to detect association with globus and reflux. Assessment of normality of data was assessed using the Shapiro Wilks test and subsequently non-parametric analyses were performed using the Mann Whitney U test.

Results: A total of 1042 upper GI endoscopies were interrogated. The use of a structured endoscopy reporting template for BRAVO capsule was used and as such all patients were classified as having the presence or absence of an inlet patch.

All patients were well sedated with a median dose of fentanyl 100mcg (75-150) and midazolam 4mg (3-7).

In all patients, CIP's were detected in 76/1042 (7.1%). Association of CIP and abnormal BRAVO reading was non-significant for number of refluxes or total acid exposure time but was significantly associated with symptoms such as chest pain ($p < 0.05$).

In those with no globus symptoms ($n=294$), CIP was detected in 13 (4.4%), but in those with globus ($n=748$), this increased to 63 (8.4%), $p=0.03$.

Conclusion: The true prevalence of cervical inlet patch may be as high as 7% and in those with oropharyngeal symptoms, over 8%. Improved detection rate may be related to numerous factors, including endoscopists level of experience at detecting pathology, sedation use and patient comfort, as well as a reporting template focusing the endoscopist to comment on presence/absence of inlet patch.

Standardised reporting templates should be considered for routine use throughout upper GI endoscopy as a potential means of enhancing quality of endoscopy.

Disclosure: Nothing to disclose

P1183

ARTIFICIAL NEURAL NETWORKS CAN DETECT THE STATE OF CONSCIOUSNESS IN SEDATION FOR ENDOSCOPY

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Introduction: In the current standard for sedation in endoscopic procedures - nurse administered propofol sedation - the drug effect is subjectively monitored by a trained nurse. Yet, current evidence suggests that the safety profile of this technique is not ideal. To date, there is no objective device to monitor sedation in endoscopic procedures.

Aims & Methods: We conducted this study to investigate the feasibility of EEG-based sedation monitoring using an artificial neural network (ANN). Standard monitoring was augmented with a two-lead frontotemporal EEG. The raw EEG data were processed to calculate a panel of 34 features, which were subsequently used training an ANN to differentiate the state of consciousness (SOC). As a benchmark, a logistic regression model was calculated. Results were cross validated to gain insight on model performance.

Results: Biosignals from 172 patients (ASA I - III) undergoing various endoscopic procedures were recorded. Single features varied in their ability to predict the SOC with a maximum area under the receiver operating characteristic curve (AUC) of 0.78. The regression model achieved a median AUC of 0.86, while the ANN achieved a median AUC of 0.88.

Conclusion: Based on the studied data we find that ANNs predict the state of consciousness with a slightly higher AUC than logistic regression models. With increasing cohort size and more advanced network architectures, prediction accuracy of ANNs is expected to further increase. Thus, we believe further investigation of this approach towards a clinical device is warranted.

Disclosure: Nothing to disclose

P1184

BRAZILIAN EXPERIENCE OF A SINGLE CENTER USING HORIZONTAL OPENING WITH VERTICAL CLOSING OF THE ESOPHAGEAL TUNNEL FOR POEM

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Introduction: Achalasia is an esophageal motility disorder characterized by loss of peristalsis in the distal esophagus and failure of lower esophageal sphincter relaxation. Endoscopic treatment options provide a significant improvement of symptoms and quality of life [1].

The treatment options today are Heller myotomy and peroral endoscopic Myotomy (POEM). Since it's first description by Inoue in 2010, the technique has spread worldwide, but there still no standardization of the procedure. The variation includes anterior or posterior myotomy, supine or lateral positioning of the patient, extension of the gastric side of the myotomy, but most services perform a vertical opening of the esophageal tunnel.

With this technique a laceration of the esophageal the mucosa occurs due to the manipulation of the endoscope, creating a larger mucosal gap and difficulty in closing, impacting on the procedure duration and higher cost due to the use of more clips.

Aims & Methods: We performed horizontal opening of the esophageal tunnel in all 1700 patients submitted to POEM in our service, with a vertical closing of the esophageal defect.

Results: With a total number of more 1700 POEMs performed since 2003, using a horizontal opening of the tunnel, we achieved less bleeding rates, easier entrance on the esophageal tunnel, smaller mucosal defect by the end of the procedure and shorter closing time, using an average of 2 clips per patient.

Conclusion: Horizontal opening of the esophageal tunnel for POEM is safe, effective, easier to perform and cheaper than the vertical option.

Disclosure: Nothing to disclose

P1185

EFFICACY AND SAFETY OF NEEDLE-TYPE KNIFE VS. SCISSORS-TYPE KNIFE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY COLORECTAL NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for treating early colorectal neoplasms. ESD knife is particularly important during this procedure, and several types of knives have been developed for its safer and more efficient performance. However, few studies have compared the efficiency and safety of different types of knives for colonic ESD.

Aims & Methods: This multicenter, prospective study aimed to evaluate the efficacy and safety of scissors- vs. needle-type knife for colonic ESD. ESD was performed for 2501 lesions (2334 patients) at 13 institutes of the Hiroshima GI Endoscopy Research Group between August 2013 and December 2018. After exclusion of 215 lesions (181 patients) removed using the snare technique, 2286 lesions (2153 patients) were included and divided into two groups: needle-type knife group (Dual Knife J, Dual Knife, or B-knife; Group A, 1849 lesions) and scissors-type knife group (SB Knife Jr or Clutch Cutter; Group B, 437 lesions). Clinicopathological findings and short-term outcomes were evaluated.

Results: Sex distribution [men: 1111 (60%) vs 268 (61%)], mean age (69 vs 70 years), and tumor location [(right / left / rectum: 957 (52%) / 381 (20%) / 511 (28%) vs 230 (52%) / 94 (22%) / 113 (26%)] and histopathology [Adenoma / Tis / T1a / T1b: 654 (35%) / 877 (47%) / 102 (6%) / 216 (12%) vs 179 (41%) / 170 (39%) / 55 (13%) / 33 (7%)] were comparable in Groups A and B.

However, the growth type (LST-G / LST-NG / Polypoid) was significantly different in Groups A and B [805 (44%) / 707 (38%) / 334 (18%) vs 176 (40%) / 155 (36%) / 106 (24%)] ($p < 0.05$). Although en-bloc / complete resection rates were similar in Groups A and B (98% / 96% vs 98% / 96%), the mean diameter of resected tumors was significantly larger in Group A (32 ± 15 mm) than in Group B (28 ± 14 mm) ($p < 0.001$).

The median procedure time was similar in Groups A and B (87 ± 71 min vs 80 ± 57 min); however, the mean ratio of the resected specimen area (diameter²) to procedure time (min) was significantly higher in Group A (13 ± 10

mm²/min) than in Group B (10 ± 9 mm²/min) ($p < 0.001$). The rate of lesions removed by ESD using only one knife was significantly higher in Group B [99% (432/437)] than in Group A [42% (727/1849)] ($p < 0.0001$).

Regarding adverse events, postoperative hemorrhage and intraoperative perforation rates were significantly higher in Group A than in Group B [2.2% (42/1849) vs 0.7% (3/437), $p < 0.05$ and 2.9% (7/1849) vs 0.7% (3/437), $p < 0.01$, respectively]. The delayed perforation rates were similar in Groups A and B [0.3% (6/1849) vs 0% (0/437)].

Conclusion: The scissors-type knife allows safer and more cost-effective lesion resection, while the needle-type knife allows faster lesion resection. Good understanding of these characteristics will permit their proper use depending on the situation.

Disclosure: Nothing to disclose

P1186

THE CLINICAL IMPACT OF HYBRID ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL TUMORS: A 10-YEAR MULTICENTER STUDY

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Introduction: Hybrid ESD of colorectal tumors is expected to reduce the procedure times relative to those required for conventional ESD. The reliable performance of hybrid ESD requires a lesion with a maximum diameter of 30 mm to ensure that the lesion fits into the snare, however no consensus has been reached on this matter to date. In addition, most studies so far have involved single institutions and few operators.

Aims & Methods: The Aim of this study was to investigate the clinical outcomes of hybrid ESD for colorectal tumors that met the indicated lesion size criterion and examine the effects of the level of operator experience on these outcomes in a multicenter study. From January 2008 to December 2018, hybrid ESD was performed in 172 lesions with tumor diameters of ≥ 20 to < 30 mm at 9 institutions in the Hiroshima area.

We compared the clinicopathological characteristics and treatment outcomes between 56 lesions in the planned hybrid ESD group and 116 lesions in the salvage hybrid ESD group. We also compared data between 2008-2013 and 2014-2018 to assess the impact of the level of operator experience.

Results: The reasons for planned hybrid ESD were to reduce the procedure time (82%), a positive non-lifting sign (9%), and an inexperienced operator (9%). Salvage hybrid ESD was performed because of poor scope operability (73%), severe submucosal fibrosis (39%), and perforation (22%). The salvage group had significantly more severe submucosal fibrosis (38.8% vs. 5.4%, respectively, $P < 0.01$) and more cases with poor scope operability (71.6% vs. 10.7%, respectively, $P < 0.0001$) than the planned group.

The procedure time was significantly longer and the perforation rate was higher in the salvage group than that in the planned group (72.0 ± 46.3 min vs. 44.5 ± 26.7 min, $P < 0.01$ and 21.6% vs. 0%, $P < 0.01$, respectively). In the salvage group, perforations occurred mostly during submucosal dissection prior to snaring (19.8%), and rarely occurred after resection of lesion (1.8%). The en bloc resection rate (94.6% vs. 87.1%) and complete en bloc resection rate (92.9% vs. 83.6%) were not significantly different between the groups. The rate of cases with poor scope operability was significantly higher during the period of 2014-2018 than during the period of 2008-2013 (68.1% vs. 32.1%, respectively, $P < 0.01$). During the second period relative to the first period, we recorded significantly higher en bloc resection rate

(98.9% vs. 78.2%, respectively, $P < 0.01$), complete en bloc resection rate (95.7% vs. 75.6%, respectively, $P < 0.01$), and experienced operators rate (75.5% vs. 53.9%, respectively, $P < 0.01$).

Furthermore, the planned group had significantly higher rates of en bloc (90.9% vs. 68.9%, respectively, $P < 0.05$) and complete en bloc resection (87.9% vs. 66.7%, respectively, $P < 0.05$) than the salvage group during the first period, whereas no significant difference was observed in the second period (en bloc resection rate: 100% vs. 98.6%, complete en bloc resection rate: 100% vs. 94.4%).

Conclusion: Hybrid ESD for suitably sized lesions is as safe as conventional ESD and can achieve high en bloc resection rates, especially when performed by experienced operators.

Disclosure: Nothing to disclose

P1187 WITHDRAWN

P1188

SMSH SCORE (SIZE, MANEUVERABILITY, SITE, HISTORY) A NEW SCORE TO PREDICT EFFICACY AND COMPLICATIONS OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)

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Introduction: ESD is the gold standard for the treatment of large colorectal superficial lesions. The SMSA score predict results of EMR for large benign lesions but no equivalent score has been designed for colorectal ESD of large superficial lesions.

The objective of this study was to identify pre-procedural predictive factors of R0 resection and perforation and try to design a predictive score.

Aims & Methods: Prospective cohort study including all cases of ESD from a French referent center between 01/2013 and 09/2019. Primary endpoint was validation of a new score that could predict R0 and non R0 resection.

Results: 507 lesions were included, 212 (41.8%) rectal lesions and 295 (58.2%) colonic.

Mean size of the lesion was 49 mm, mean procedure time was 109 min. 8 lesions were recurrent adenomas post EMR and 1 was a post surgery adenoma recurrence.

The en bloc, R0 and curative resection rates were 94.5%, 80.5% and 75.7%, respectively.

In multivariate analysis: size (OR: 0.982, $p = 0.002$), poor endoscopic maneuverability (OR: 0.390, $p = 0.001$), were significant pre-procedure risk factors for non-R0 resection.

A new score called SMSH (Size-Maneuverability-Site-History) was created to predict through pre-procedure criteria the effectiveness of colorectal ESD (Table 1).

This score is divided into 4 groups 1 (< 4 points); 2 (4 points); 3 (>4 and < 8 points); 4 (>=8 points) of increasing difficulty.

Applied to our prospective cohort 137 (27%) patients were classified as SMSH 1, 121 SMSH 2 (24%) and 159 SMSH 3 (31.4%) and 90 SMSH 4 (17.8%) There was a significant difference between the 3 groups:

- En bloc resection rate: SMSH 1: 98.5% SMSH 2: 98.3% SMSH 3: 93% and SMSH 4: 85.6% $p < 0.0001$

- R0 resection rate: SMSH 1: 91.2% ; SMSH 2: 86.8% ; SMSH 3: 75.5% ; SMSH 4: 64.4% $p < 0.0001$

- Perforation rate: SMSH 1 : 5.1% ; SMSH 2 : 10% ; SMSH 3 : 9.4%; SMSH 4: 16.7% $p < 0.0001$

Size	Manoeuvrability	Site	History
0: <4cm	0: good manoeuvrability	0: Rectum	0: naive lesion
4: 4 to 7cm	4: poor manoeuvrability	2: "simple colon"	2: IBD, radiotherapy
8: >7 cm		4: sigmoid, anal verge, hepatic flexure	4: post EMR recurrence
		8: ileon	8: post surgery recurrence

[SMSH (Size, Manoeuvrability, Site, History) score]

Conclusion: SMSH score is a new score designed thanks to the largest european colorectal ESD cohort and is able to predict results of colorectal ESD based on pre-procedural data. This new score should to help physicians to target their lesions according to their expertise. Independent validation cohort is needed.

Disclosure: Nothing to disclose

P1189

ENDOSCOPIC SUBMUCOSAL DISSECTION USING SCISSOR TYPE KNIFE (SB KNIFE) FOR LARGE BROAD-BASED OR STALKED COLONIC POLYPS: A MULTICENTRE CASE SERIES

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Introduction: Large, broad-based or stalked polyps can be technically difficult to resect with significant risk of intraprocedural and delayed bleeding. We report our experience in endoscopic submucosal dissection (ESD) using a scissor-type monopolar knife (SB-knife Junior, Sumius) for pedunculated (Ip) and sub-pedunculated (Isp) polyps.

Aims & Methods: Prospective databases from four institutions including 57 consecutive patients with 61 polyps (Ip n=38/Isp n=23) resected by ESD with SB-knife between 2014 and 2019 were analysed. Intra-procedural bleeding was treated with the haemostatic function of SB-knife. Clinicopathological characteristics, additional instrument exchange for haemostasis and complication rates were examined.

Results: Median polyp size was 35mm (20-70mm). Fifty-one polyps (84%) were in rectum/sigmoid colon. Histology showed: 30 adenomas with low-grade dysplasia (49%), 19 adenomas with high-grade dysplasia (31%), four T1N0 adenocarcinomas (7%), three serrated lesions (5%), three hamartomas (5%) and two lipomas (3%). En-bloc resection was achieved for 57 polyps (95%). Three Isp lesions were switched to piecemeal snare-resection after partial SB-knife dissection. One ESD was abandoned as muscle retraction was noted during dissection. At surgery, this patient had a T1N0 (SM3) tumour. Complete histological (R0) resection rate was 91% (52/57). Two cases had unevaluable margins (RX) and one case had deep margin

involvement (R1). Of three polyp cancers, one had a curative (R0) result at index resection with SB-knife whilst two patients at risk of lymph node metastasis underwent additional radical surgery. Haemostatic forceps were required during in 11 ESD cases (18%). Prophylactic clips were used in 54 (89%) cases (median 4 clips (range 1-10)). There were no episodes of perforation or post-polypectomy bleeding. Twenty-nine patients (51%) had endoscopic follow-up data over a median 12 months (range 6-48). One piecemeal resected polyp had local recurrence at 6 months, treated successfully with under-water EMR.

Conclusion: ESD with the SB-knife is efficient and safe in treating Ip/Is polyps. Our series highlighted a favourable short and medium-term outcome.

Disclosure: Nothing to disclose

P1190

A PROOF-OF-CONCEPT STUDY FOR AN ARTIFICIAL-INTELLIGENCE-ASSISTED CHARACTERIZATION SYSTEM FOR NARROW-BAND IMAGING COLONOSCOPY

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Introduction: Precise optical biopsy of colorectal polyps could improve the cost-effectiveness of colonoscopy and reduce polypectomy-related complications. The European Society of Gastrointestinal Endoscopy guidelines suggest that optical biopsy of diminutive polyps using narrow-band imaging (NBI) or other image-enhanced techniques could potentially replace conventional pathological diagnosis under strictly-controlled conditions. However, despite standardized training or sufficient expertise, it remains difficult to achieve sufficient diagnostic performance to characterize colorectal polyps, clinically. To address this limitation, artificial intelligence (AI)-assisted computer-aided diagnosis (CADx) is receiving attention.

Aims & Methods: Our aim was to develop AI-assisted, fully-automated CADx for colorectal polyps using NBI and to evaluate its diagnostic performance. This study was a single-center retrospective proof-of-concept study.

This new system comprised two algorithms: computer-aided detection (CADE), which can detect and extract the area of the colorectal polyp from an endoscopic image, and CADx, which outputs a pathological prediction (adenoma or non-adenoma) by analyzing the extracted candidate polyp NBI image. Although the system was a prototype, it was designed to be user-friendly; when the endoscopists captured the polyp NBI image, the image was preprocessed by the system and an output CADx diagnosis was generated automatically. Regarding the training of the algorithm, we performed two steps.

First, we used a previously developed CADE system (Misawa et al, Gastroenterology, 2018) and retrained the system with 64 448 images.

Second, we trained the CADx system using transfer learning and VGG16 which is one of the most common deep convolutional neural networks.

We prepared 2896 images taken from 427 tubular adenomas and 1113 images from 162 hyperplastic polyps as training samples for the CADx. We derived the evaluation samples by randomly extracting 100 colorectal polyp images from the endoscopy database according to the following criterion: patients with small polyps (< 10 mm) confirmed on colonos-

copy performed between January 2016 and July 2017. The exclusion criteria were sessile serrated lesions, nonepithelial lesions, inflammatory bowel disease, and lesions with no associated NBI image. All images in this study were obtained using high-definition cameras. The outcome measures were sensitivity, specificity, negative predictive value (NPV), and accuracy.

Results: The 100 polyps for the test set were extracted from 89 patients, and the median size of the lesions was 5 mm. Histopathological evaluation confirmed that 64 lesions (64%) were adenomatous, and 36 lesions (36%) were non-adenomatous (hyperplastic or inflammatory polyps). Among the lesions, one adenoma and one hyperplastic polyp were mis-detected or mis-localized by the CADE algorithm. These lesions were treated as wrong diagnoses (worst-case scenario). The sensitivity, specificity, NPV, and accuracy of the system to diagnose adenomatous lesions was 98.4%, 58.3%, 95.5%, and 85%, respectively.

Conclusion: We proved the concept of an AI-assisted automated characterization system for NBI images. Although the system was a prototype, it achieved sufficient sensitivity and NPV for adenomas to possibly allow the system to replace conventional pathological diagnosis.

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P1191

RISK OF COLORECTAL CANCER AND ADVANCED POLYPS ONE YEAR AFTER EXCISION OF HIGH-RISK ADENOMAS

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Introduction: Patients with ≥ 5 adenomas or at least one adenoma ≥ 20 mm are classified as high-risk and recommended to undergo one-year surveillance colonoscopy after index procedure according to the European guidelines for quality assurance in colorectal cancer (CRC) prevention. However, data supporting this recommendation are not entirely consistent.

Aims & Methods: To evaluate the risk of CRC, advanced adenoma and advanced serrated polyps at one-year surveillance colonoscopy in high-risk patients.

Multicenter cohort study in FIT-based CRC screening programs in Spain. Participants between January 2014 and December 2015 with at least one adenoma ≥ 20 mm or ≥ 5 adenomas of any size were included. Absolute risk

of CRC, advanced adenomas and advanced serrated polyps at one-year surveillance colonoscopy was calculated. Univariate and multivariate logistic regression analysis was performed to evaluate risk factors for advanced neoplasia at follow-up.

Results: A total of 2,119 high-risk patients were included. At one year, a total of 6 CRC (0.3%), 228 advanced adenomas (10.5%) and 58 advanced serrated polyps (2.7%) were found. In the multivariate analysis, having ≥ 5 adenomas (OR 1.53; 95% CI 1.15-2.03; p 0.004) or proximal polyps (OR 1.52; 95% CI 1.15-2.02; p 0.004) were associated with the finding of advanced neoplasia at follow-up.

Conclusion: Risk of CRC at one year is low between patients classified at high risk in the European Guidelines of surveillance after adenoma resection. The highest risk of advanced neoplasia at follow-up was found in patients with 5 or more adenomas or proximal polyps at baseline.

Disclosure: Nothing to disclose

P1192

AN INTERNATIONAL MULTICENTRE RANDOMISED CONTROLLED TRIAL OF LINKED COLOR IMAGING VERSUS HIGH-DEFINITION WHITE LIGHT ENDOSCOPY FOR POLYP DETECTION IN PATIENTS WITH LYNCH SYNDROME (LCI LYNCH)

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Introduction: Despite regular colonoscopic surveillance, interval colorectal cancers (CRC) still occur in patients with Lynch syndrome. These cancers may develop from missed polyps. Linked Color imaging (LCI) is a push-button endoscopic imaging technique developed to enhance the vasculature and architecture of the mucosal surface by narrowing the spectrum of absorbed light. This could potentially increase the detection of polyps.

The aim of this study was to assess if LCI is superior to HD-WLE for the detection of polyps during surveillance colonoscopy in patients with Lynch syndrome.

Aims & Methods: This prospective, randomised controlled trial was performed in eight international centres. Consecutive Lynch syndrome patients undergoing a surveillance colonoscopy were randomised for inspection with either LCI or HD-WLE. Eligible patients were 18 years or older

and diagnosed with a Lynch syndrome-associated pathogenic gene variant (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *Epcam*). Randomisation (1:1) was stratified by centre and performed prior to the start of colonoscopy. Patients with a Boston Bowel Preparation Scale (BBPS) < 6 or an incomplete colonoscopy were excluded after randomisation. Participating endoscopists had intensive experience ($> 2,000$ colonoscopies) and were familiar with LCI (> 10 LCI procedures). The primary outcome was the proportion of patients with at least one polyp detected during colonoscopy (polyp detection rate). To demonstrate superiority of LCI over HD-WLE a total of 332 patients were required (absolute increase polyp detection rate from 25% to 40%; power 80%; α .05).

Results: Between January 2018 and March 2020, 357 patients were randomised to undergo inspection with LCI or HD-WLE. After excluding 25 patients (6 incomplete colonoscopy and 19 BBPS < 6), 332 patients were included in the analysis (160 LCI group, 172 HD-WLE group). The baseline characteristics were similar in the two groups. The mean age of patients was 48.4 years (SD 14.1), 42% were male, 22% had a history of CRC and the median time since the previous colonoscopy was 17 months (IQR 13-24). No significant difference was observed between the polyp detection rate in the LCI group (44%; 95% CI 37-52%) compared with the HD-WLE group (36%; 95% CI 29-44%) ($P=.12$). The adenoma detection rate in the LCI group (35%; 95% CI 29-44%) was significantly higher compared to the HD-WLE group (26%; 95% CI 19-33%) ($P=.04$).

Also, the mean number of polyps per patient (0.94 vs. 0.62; $P=.03$) and the mean number of adenomas per patient (0.65 vs. 0.42; $P=.04$) were significantly higher in the LCI group than in the HD-WLE group. A significant higher proportion of patients with proximal adenomas (26% vs 19%; $P=.04$) and ≤ 5 mm adenomas (30% vs 22%; $P=.03$) were detected in the LCI group compared to the HD-WLE group.

There were no significant differences between groups in proportion of patients with flat adenomas (17% vs 12%; $P=.18$), sessile serrated lesions (7% vs 7%; $P=.97$), hyperplastic polyps (10% vs. 9%; $P=.56$) or advanced adenomas (4% vs 5%, $P=.90$). No significant differences were observed in the median procedure and extubation times between the LCI and HD-WLE group: 23 vs. 22 min ($P=.44$) and 15 vs. 13 min ($P=.09$), respectively.

Conclusion: In this multicentre randomised controlled study, the use of LCI did not improve polyp detection rate compared to HD-WLE in Lynch syndrome patients. However, LCI did increase the adenoma detection rate and the mean number of adenomas detected per patient, and might therefore be of benefit for patients with Lynch syndrome (NCT03344289).

Disclosure: Fujifilm Europe GmbH provided research equipment on loan for this study and an unrestricted research grant for this study. E. Dekker received equipment on loan from Olympus, a consulting fee for medical advice from Tillots, Olympus, Fujifilm, GI Supply and CPP-FAP and a speakers' fee from Olympus, Roche and GI Supply. M. Pellisé received research grant from Fujifilm, received consultancy fee from Norgine, speaker's fee from Norgine, Olympus, Casen Recordati, Janssen and editorial fee from Thieme. P. Fockens received personal fees from Cook, Ethicon and Olympus, research support from Boston Scientific. R. Bisschops has provided consultancy to and received research grants and speaker's fees from Pentax (2008 to present) and Fujifilm (2015 to present); his department has received research grants and equipment from Pentax (2015 to present). M.F. Kaminski has received speaker's, teaching, and consultancy fees from Olympus (2017 to present) and speaker's and teaching fees). P. Bhandari has received grant funding from Norgine. A. Repici received consultancy fee from Medtronic. Other authors have no disclosures.

P1193

RESULTS OF ADDITIONAL SURGERY AFTER ENDOSCOPIC RESECTION FOR T1 COLORECTAL CANCER IN A FRENCH MULTICENTER COHORT

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Introduction: The progress made over the past ten years in therapeutic endoscopy allows treating superficial colorectal cancers with low morbidity and almost no mortality. However, a 10% risk of lymph node involvement is associated with submucosal (T1) colorectal carcinomas, potentially indicating additional surgical resection. The absence of four histological features recalled in the Japanese (JSCCR) and European (ESGE) guidelines (submucosal infiltration >1000µm, lymphovascular invasion, grade 2-3 tumor budding, poor tumor differentiation) allows in case of R0 resection to predict a very low risk of lymph node involvement, and thus to avoid additional surgery with lymph node dissection. Since the vast majority of the studies were conducted in Japan, we aimed to evaluate the results of complementary surgery after endoscopic resection for a T1 colorectal cancer in a Western population.

Aims & Methods: We conducted a retrospective multicenter study and included all patients who had an endoscopic mucosal resection or an endoscopic submucosal dissection for T1 colorectal cancer in twelve French expert centers between March 2012 and July 2019. All cases were discussed in a multidisciplinary meeting. Demographic, clinical, endoscopic and histological data were collected.

Results: We included 353 patients. The mean ± SD age of the population was 67.5 ± 11.0 years. About half of the lesions were in the colon (49.3%) and half in the rectum (50.7%). Nearly half of the patients had an endoscopic submucosal dissection. Complementary surgery and surveillance alone were recommended in 46.2% and 53.8% of patients, respectively. Surgical and histological data were available for 145 patients. Four patients were operated without any pejorative histological feature and examination of the surgical specimens did not show lymph node involvement. Of the 141 patients who had an actual indication for additional surgery according to the guidelines, 112 (79.4%) had a pT0N0 surgical specimen despite the existence of an undifferentiated cancer, a grade 2-3 budding, a lymphovascular invasion or a deep submucosal invasion on the endoscopic resection specimen. 10 (7.1%) patients had a local tumor residue and of these, 7 had a histological R1 endoscopic resection. 24 (17.0%) patients had lymph node metastases. When deep submucosal invasion was the only pejorative histological feature, lymph node involvement was found only when submucosal invasion was deeper than 2000 µm.

Conclusion: Using the histological criteria recommended by the JSCCR to indicate a complementary surgery after endoscopic resection for T1 colorectal cancer in a Western population leads to 79% of surgical speci-

mens free of cancer. In this study, pushing the threshold of submucosal invasion up to 2000 µm associated with the absence of any pejorative qualitative histological feature could reduce the number of surgical indications without increasing the risk of lymph node involvement. Other histological features predictive of the risk of lymph node metastases are needed.

Disclosure: Nothing to disclose

P1194

SCREENING COLONOSCOPY IN THE UNDER 50 YEARS POPULATION DETECTS A HIGHER RATE OF SERRATED LESIONS COMPARED TO THE POPULATION OVER 50

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Introduction: While the incidence of Colorectal cancer (CRC) is decreasing among individuals over 50 years it is increasing within younger adults. A study by Reinier et al showed that CRC among young adults is diagnosed at a later stages, However, it is still unknown if there are differences among precursor lesions between adults under the age of 50 compared to those above, which might be able to explain such findings.

Aims & Methods: 36.582 screening colonoscopies between 2007 and 2019 were assessed within the Austrian quality assurance program. Main reason for undergoing colonoscopy within asymptomatic individuals under the age of 50 was fear of cancer. The proportion of different types of adenomas between patients aged < 50 and ≥ 50 was compared within this study.

Results: 336.582 screening colonoscopies were analyzed. 12.256 (3,6%) of patients were under the age of 50 and 324.326 (96,4%) above. Adenomas were detected in 12,5% (n=1.531) within individuals < 50 years and in 23,7% (n=76.742) within above. 9,5% (n=146) of adenomas among adults under 50 years were sessile serrated adenomas (SSA) compared to 6,5% (n=4951) among those older than 50 (p< 0,001). 2,9% (n=45) were traditional serrated polyps (TSA) in the age group <50 compared to 1,2% (896) in age group ≥ 50 (p< 0,001).

Proportion of tubular adenomas was 71,1% (n=1089) within individuals <50 years and 76,2% (n=58.480) within patients older than 50 years (p< 0,001). 15,5% (n=238) vs. 15,3% (11.766) of adenomas were tubulovillous (p=0,81) and 0,8% (n=13) vs. 0,8% (n=639) were villous adenomas (p=0,89) comparing <50 and ≥ 50 year-old individuals (p=0,81).

Conclusion: Pathologists and Clinicians should be aware that individuals younger than 50 years might have higher proportions of SSAs, as well as TSAs, compared to individuals older than 50. In contrast the proportion of tubular adenomas was significant lower among 20-49 year old patients. There was no difference in proportion of tubulovillous and villous adenomas.

Disclosure: Nothing to disclose

P1195

COST SAVINGS IN COLONOSCOPY WITH ARTIFICIAL INTELLIGENCE-AIDED POLYP DIAGNOSIS: AN ADD-ON ANALYSIS OF A CLINICAL TRIAL

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Introduction: Artificial intelligence (AI) is being implemented into colonoscopy practice, but no study has investigated whether AI is cost-saving. We quantified the cost reduction from using AI as an aid in the optical diagnosis of colorectal polyps.

Aims & Methods: This study is an add-on analysis of a clinical trial [1] that investigated the performance of AI for differentiating colorectal polyps (i.e., neoplastic versus non-neoplastic). We included all patients with diminutive (≤ 5 mm) rectosigmoid polyp for analyses. The average colonoscopy cost was compared for two scenarios: A) a diagnose-and-leave strategy supported by the AI prediction (i.e., diminutive rectosigmoid polyps were not removed when predicted as non-neoplastic), B) a resect-all-polyps strategy. Gross annual costs for colonoscopies were also calculated based on numbers and reimbursement of colonoscopies conducted under public health insurances in four countries.

Results: Overall, 207 patients with 250 diminutive rectosigmoid polyps (104 neoplastic, 144 non-neoplastic, and two indeterminate) were included. AI correctly differentiated neoplastic polyps with 93.3% sensitivity, 95.2% specificity, and 95.2% negative predictive value. Thus, 105 polyps were removed while 145 were left under the diagnose-and-leave strategy, which was estimated to reduce the average colonoscopy cost and the gross annual reimbursement for colonoscopies by 18.9% and 149.2 million dollars in Japan, 6.9% and 12.3 million dollars in England, 7.6% and 1.1 million dollars in Norway, and 10.9% and 85.2 million dollars in the United States, respectively, compared to the resect-all-polyps strategy.

Conclusion: The use of AI to enable the diagnose-and-leave strategy results in substantial cost reductions for colonoscopy. Thus, clinical implementation of AI-assisted optical biopsy may be encouraged, together with reimbursement support from public health insurance bodies.

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Disclosure: YM and MM have received speaking honoraria from Olympus Corp. JEE is the consultant of Satisfai Health. AR have received a research grant from Olympus Corp. AR is the consultant of Cook Medical and Boston Scientific Corp. KM received research funding from Cybernet Corp. None of the other authors have conflicts of interest relating to the present study.

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ARTIFICIAL INTELLIGENCE COMBINED WITH LCI YIELDS IN HIGHEST ACCURACY AND DETECTION OF COLORECTAL POLYPS, INCLUDING SESSILE SERRATED LESIONS

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Introduction: Linked color imaging (LCI) has shown its effectiveness in multiple randomized controlled trials for enhanced colorectal polyp detection. Most recently, artificial intelligence (AI) with deep learning through convolutional neural networks has dramatically improved and is increasingly recognized as a promising new technique enhancing colorectal polyp detection.

Aims & Methods: Study aim was to evaluate a new developed deep-learning computer-aided detection (CAD) system in combination with LCI for colorectal polyp detection.

First, a convolutional neural network was trained for colorectal polyp detection in combination with the LCI-technique using a dataset of anonymized endoscopy videos. For the validation, 240 polyps within fully recorded endoscopy videos with LCI mode, covering the whole spectrum of adenomatous histology, were used. Sensitivity (True positive rate per lesion) and false positive frames in a full procedure were assessed.

Results: The new CAD system used on LCI mode could at least process 60 frames per second allowing for real-time video analysis. Sensitivity (True positive rate per lesion) was 100% with no lesion being missed. The calculated false positive frame rate was 0.001%. Out of the 240 polyps included, 34 were sessile serrated lesions. The detection rate for sessile serrated lesions with the CAD system used on LCI mode was 100%.

Conclusion: The new CAD system used on LCI mode achieved a 100% sensitivity per lesion and a negligible false positive frame rate. Of note, the new CAD system used on LCI mode also specifically allowed for detection of serrated lesions in all cases.

Disclosure: Nothing to disclose

P1197

CHARACTERISATION OF COLORECTAL POLYPS USING ARTIFICIAL INTELLIGENCE, FUTURE IS ALREADY HERE!

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Introduction: Optical diagnosis of polyps using electronic chromoendoscopy has been proven to be very accurate in expert hands. However, it has never worked outside of expert centres and a huge inter-observer variation has been reported. Due to this reason, despite recommendations from all International societies, the strategy of 'resect & discard' has not been implemented in any country. Artificial intelligence has been reported to be very effective in detecting polyps but data on optical diagnosis is very limited.

Aims & Methods: The aim of this study was to evaluate the diagnostic performance of a recently developed AI system for polyp detection and characterisation (EW10-EC02 CAD-EYE system from Fujifilm Japan). This is

the only CE marked and commercially available system for real time characterisation of polyps. The AI model was developed using convolutional neural networks CNN. It was pre trained on 5000 images for detection and characterisation of colorectal polyps. We assessed this system on real time video recordings of colorectal polyps. All procedures were performed using Fujifilm ELUXEO™ 7000 platform. All polyps were assessed with white light and blue light imaging (BLI). Characterisation was done on BLI mode. All polyps had histological diagnosis which was used as the ground truth to assess the system accuracy.

Results: Video recordings of 60 polyps of varying sizes were used in this study. These included 27, 16, and 17 polyps of < 5mm, 5-10mm, and >10mm respectively. Forty four (73.3%) polyps were in the left colon, and 20 (33.3%) had flat morphology. Histological diagnosis was non-neoplastic (hyperplastic & SSP) and neoplastic (adenomas) in 31 and 29 polyps respectively. The CAD EYE system detected all polyps and predicted accurate histological diagnosis with 93.3% overall accuracy. The sensitivity was 93.1%, specificity 93.5%, and NPV was 93.5%. Polyps that were wrongly predicted (n=4) were equally distributed between flat and non flat, and hyperplastic and neoplastic histology.

Conclusion: This AI system detected and diagnosed colorectal polyps on recorded endoscopy videos with high degree of accuracy, regardless of polyp size, morphology or location. If proven in real time studies, this could support the implementation of resect and discard strategy, with significant clinical and cost implications.

Disclosure: Nothing to disclose

P1198

GREATER HIGH-QUALITY RIGHT COLON CLEANSING WITH 1L NER1006 VERSUS 2L POLYETHYLENE GLYCOL + ASCORBATE OR ORAL SULFATE SOLUTION IN ALL PATIENTS WITH RIGHT COLON SCORES BY CENTRAL READERS: A POST-HOC ANALYSIS OF TWO RANDOMIZED CONTROLLED PHASE 3 CLINICAL TRIALS

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Introduction: NER1006 is the first 1L polyethylene glycol (PEG)-based bowel preparation. In two randomized controlled phase 3 clinical trials, NER1006 demonstrated non-inferior overall colon cleansing success and high-quality right colon cleansing success compared to 2L PEG+ ascorbate (2LPEG; MORA trial) and oral sulfate solution (OSS; NOCT trial) [1,2]. In patients with full segmental scoring by site endoscopists, NER1006 also showed superior high-quality overall colon cleansing success versus both 2LPEG and OSS [3]. Site endoscopists and central readers independently scored more high-quality cleansed segments in patients using NER1006 versus 2LPEG or OSS [3,4].

Since high-quality cleansing in the right colon using the validated Harefield Cleansing Scale (HCS) was also an alternative primary endpoint in the primary trials, we analysed the comparative right colon high-quality cleansing efficacy in study patients who underwent a colonoscopy and also had their right colons scored.

Aims & Methods: A post-hoc analysis of the MORA and NOCT trials was performed to assess the superiority of high-quality right colon cleansing by NER1006 versus 2LPEG and OSS. Patients included in both trials were males and females aged 18-85 years. They were randomized to receive NER1006, 2LPEG, or OSS as a two-day evening/morning split-dosing regimen (N2D) or NER1006 as a same-day morning-only dosing regimen (N1D).

This analysis included all randomized patients who underwent colonoscopy with right colon cleansing scoring by treatment-blinded central readers using the HCS. Patients with documented segmental scorings better represent the patient population undergoing colonoscopy in real-world clinics. High-quality cleansing is defined as a segmental score of 3 (stool-free) or 4 (empty and clean) on a scale 0-4 and must be assigned without any intraprocedural washing being required. High-quality cleansing success rates were calculated and compared using the 1-sided t-test.

Results: 792 of 822 (96% MORA) and 515 of 556 (93% NOCT) randomized patients were included in this analysis. Within each trial, the baseline characteristics were comparable between the treatment groups. Mean age of the patients included in each treatment group was in the range of 54-58 years. Both regimens of NER1006, N2D and N1D achieved greater right colon high-quality cleansing success rates compared to 2LPEG [87/262 (33.2%) and 93/270 (34.4%) versus 41/260 (15.8%); P<0.001 for both comparisons] (Table 1).

Similarly, NER1006 achieved greater high-quality cleansing success rates compared to OSS [99/255 (38.8%) versus 82/260 (31.5%); P=0.042]. Safety was comparable with no treatment-related serious adverse events in any group.

Conclusion: In patients who underwent colonoscopy and had their right colons scored by treatment-blinded central readers, the 1L NER1006 attained superior high-quality right colon cleansing compared to both 2LPEG and OSS.

	MORA			NOCT	
	N2D	N1D	2LPEG	N2D	OSS
Sample size, N	262	270	260	255	260
High-quality right colon cleansing success, % (n/N)	33.2% (87/262)	34.4% (93/270)	15.8% (41/260)	38.8% (99/255)	31.5% (82/260)
1-sided p-values versus comparator	P<0.001	P<0.001		P=0.042	

[Table 1. Right colon high-quality cleansing success rates in patients who had a colonoscopy with their colon assessed by central readers using HCS.]

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THE SWEDISH STANDARDIZED COURSE OF CARE - COLORECTAL CANCER PREVALENCE AND PREDICTIVE VALUE OF ENTRY CRITERIA

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Introduction: To improve the efficacy of cancer diagnosis and treatment, fast tracks were implemented in Sweden in 2015. The fast tracks are called standardized course of care (SCC). The SCC for colorectal cancer (CRC-SCC) was implemented in 2016. Since then, about 46.000 patients have been examined according to the CRC-SCC and 27% of these have initiated treat-

ment. The entry criteria for colonoscopy with respect to CRC comprise: visible blood in stool, radiological abnormality, onset of altered bowel habits > 4 weeks in patients above 40 years, abnormal rectal examination and anemia of unknown cause. If a patient fulfills one or more of these criteria, a colonoscopy should be performed within 10 days.

Aims & Methods: The aim of the study was to identify the prevalence of CRC among patients referred to the University Hospital of Örebro (USÖ) according to the CRC-SCC. We also investigated the positive predicting values (PPVs) and odds ratios (ORs) of different SCC-entry criteria with respect to CRC. We performed a medical record- and referral review, including all patients examined with colonoscopy, according to the CRC-SCC at the USÖ between September 2016 and December 2018 (n=1271).

Results: CRC was found in 15.3% of all patients. The PPVs of SCC-criteria for CRC were generally low with the highest ones for abnormal rectal examination (29.7%), abnormal radiology (29.2%) and anemia of unknown cause (21.3%). These were also the only criteria with a statistically significant increased risk for CRC, OR 2.8 (95% CI 2.0-4.1), 2.8 (95% CI 1.9-4.0) and 1.7 (95% CI 1.2-2.4), respectively. In 52% of the CRC-SCC-referrals, altered bowel function was the predominant symptom. However, this symptom was not associated with an increased risk for CRC, OR 0.6 (95%CI 0.5-0.9). A negative fecal occult blood test (FOBT) showed a high negative predictive value for CRC (99.5%). However, only 53% of the referrals included a FOBT.

SCC-criteria	No cancer (n=1077)	Cancer (n=194)	PPV	OR (95% CI)	P-value
	n (%)	n (%)			
Altered bowel function	581 (53.9)	82 (42.3)	12.4%	0.6 (0.5-0.9)	0.003
Abnormal radiology	126 (11.7)	52 (26.8)	29.2%	2.8 (1.9-4.0)	<0.001
Abnormal rectal examination	123 (11.4)	52 (26.8)	29.7%	2.8 (2.0-4.1)	<0.001
Rectal bleeding	227 (21.1)	33 (17.0)	12.7%	0.8 (0.5-1.2)	0.20
Anemia of unknown cause	230 (21.4)	62 (32.0)	21.3%	1.7 (1.2-2.4)	0.001

[Frequencies, positive predictive values and odds ratios for different criteria of the standardized course of care for colorectal cancer]

Conclusion: CRC was found in 15.3% of the patients referred according to the CRC-SCC to the USÖ during the time period 2016-2019. This number is lower than expected. A possible explanation includes a heterogeneity in both the writing and assessment of the referrals, resulting in colonoscopies that were performed in patients who did not actually met the entry criteria.

The PPVs of SCC-criteria for CRC were generally low. More than half of the patients were referred due to altered bowel function. This symptom was, however, not associated with an increased CRC-risk. Adding a FOBT to the CRC-SCC before referring patients for a colonoscopy could improve diagnostic efficacy.

Disclosure: Nothing to disclose

P1200

SALVAGE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LOCAL RESIDUAL/RECURRENT COLORECTAL TUMOR AFTER ENDOSCOPIC RESECTION: A LARGE MULTICENTER STUDY

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Introduction: In local residual/recurrent and endoscopic resection (ER) interrupted colorectal tumors, endoscopic retreatment using endoscopic mucosal resection (EMR) is often difficult due to severe submucosal fibrosis. Endoscopic submucosal dissection (ESD) can achieve en bloc resection even for tumors with severe submucosal fibrosis, although it is a risk factor of incomplete resection and perforation. This study aimed to evaluate the efficacy and safety of colorectal ESD for local residual/recurrent tumor including ER interrupted tumor.

Aims & Methods: From January 2008 until December 2018, 3,937 colorectal tumors were resected by ESD, at the Hiroshima GI Research Group, comprising an academic hospital and 24 community hospitals with different levels of experience in colorectal ESD. From this group, 81 local residual/recurrent tumors and 21 ER interrupted tumors were included in this study. Of 81 local residual/recurrent tumors, 77 had previously undergone EMR (including 15 piecemeal resections). ESD or polypectomy had been performed in three and one cases, respectively. The mean period from the previous ER to salvage ESD was 29 months (range, 1-132 months). Of 21 ER interrupted tumors, 19 were interrupted during EMR; 15 and 4 were due to positive non-lifting sign and due to poor endoscope operability, respectively. Moreover, two were interrupted during ESD due to uncontrolled intraoperative bleeding or poor endoscope operability. The mean period from the previous interrupted ER to salvage ESD was 2 months (range, 1-13 months). The ESD outcomes, namely the difference between the early and late phases and re-recurrence after ESD for local residual/recurrent tumor were evaluated.

Results: For local residual/recurrent tumor, en bloc and R0 resection rates were 95% (77/81) and 90% (73/81), respectively. All of 4 cases with piecemeal resection were low-grade dysplasias (LGDs). Four cases with en bloc resection but non-R0 resection were due to a positive vertical margin of submucosal deep invasive carcinoma being present. Intraoperative and delayed perforations occurred in 5 and 2 cases, respectively, and 2 of them required surgery. For ER interrupted tumors, both the en bloc and R0 resection rates were 86% (18/21), with no major adverse events. In three tumors with piecemeal resection, 1 was classified as high-grade dysplasia and 2 as LGDs. Intraoperative perforation rate of the late phase was 2%, which was significantly lower than that of the early phase (11%). Of the 72 curative resection cases for local residual/recurrent tumor, surveillance colonoscopies were performed in 67 cases (93%), and local re-recurrences were not observed during the 33 months of the median follow-up period. Five out of 9 non-curative resection cases were due to submucosal deep invasive carcinoma; 1 case was followed up without surgery due to lung cancer comorbidity resulting in death 18 months after ESD, and the other

4 underwent additional surgeries (3 were negative, but 1 was positive for lymph node metastasis receiving subsequent chemotherapy). The other 4 out of 9 non-curative resection cases were due to piecemeal resection of LGD, and were followed up without surgeries and no local re-recurrences were observed during the 60 months of the median follow-up period.

Conclusion: Colorectal ESD is a reliable treatment for local residual/recurrent and ER interrupted tumors, providing high en bloc resection and low recurrence rates.

Disclosure: Nothing to disclose

P1201

PROPOFOL SEDATION DOES NOT IMPROVE MEASURES OF COLONOSCOPY QUALITY - FINDINGS FROM THE SOUTHWEST ONTARIO COLONOSCOPY COHORT

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Introduction: Prior studies examining the use of propofol sedation during colonoscopy have focused on anesthesia outcomes. Whether propofol sedation is associated with improved colonoscopy outcomes compared to conscious sedation is unknown and was the objective of this study.

Aims & Methods: The Southwest Ontario Colonoscopy cohort consists of all patients who underwent colonoscopy between April 2017 and Oct 2018 at 21 hospitals serving a large geographic area in Southwest Ontario. Procedures done in patients < 18 years of age or by an endoscopist performing < 50 colonoscopies/year were excluded. Data were collected through a mandatory quality assurance form that was completed by the endoscopist after each procedure. Pathology reports were manually reviewed. The primary outcome was the adenoma detection rate (ADR). Secondary outcomes included the detection rate of any adenoma (conventional adenoma, sessile serrated polyp, and traditional serrated adenoma), sessile serrated polyp detection rate, polyp detection rate, cecal intubation rate, and perforation rate. Unadjusted outcome rates were described. Rates were modeled using modified Poisson regression adjusting for clustering at the level of the physician adjusting for propofol use versus conscious sedation. Additional factors adjusted for included subject characteristics (including age, sex, ASA grade), procedure characteristics (indication for procedure, bowel preparation quality, outpatient setting, split dosing, trainees present) and physician characteristics (years of experience, specialty and academic setting).

Results: A total of 46,634 colonoscopies were performed by 75 physicians (37.5% by gastroenterologists, 60% by general surgeons, 2.5% others), of which 16,408 (35.2%) received propofol and 30,226 (64.8%) received conscious sedation (e.g. a combination of a benzodiazepine and a narcotic).

Patients who received propofol were more likely to have a screening indication (48.6% vs. 43.7%, $p<0.0001$), not have a trainee present (93.7% vs. 83.5%, $p<0.0001$), and be performed at a non-academic centre (69.3% vs. 51.6%, $p<0.001$).

Compared to conscious sedation, use of propofol on crude analysis was associated with a lower ADR (24.6% vs. 27.0%, $p<0.0001$) and detection of any adenoma (27.7% vs. 29.8%, $p<0.0001$), but not sessile serrated polyp detection rate (5.0% vs. 4.7%, $p=0.26$), polyp detection rate (41.2% vs 41.2%, $p=0.978$), cecal intubation rate (97.1% vs. 96.8%, $p=0.15$) or perforation rate (0.04% vs. 0.06%, $p=0.45$). On multi-variable analysis, there was no difference between use of propofol or conscious sedation for ADR (RR=0.90, 95% CI 0.74-1.10, $p=0.30$), detection of any adenoma (RR=0.93, 95% CI 0.75-1.14, $p=0.47$), sessile serrated polyp detection rate (RR=1.20, 95%CI 0.90-1.60, $p=0.22$), polyp detection rate (RR=1.00, 95% CI 0.90-1.11, $p=0.99$), or cecal intubation rate (RR=1.00, 95%CI 0.80-1.26, $p=0.99$).

Conclusion: The use of propofol sedation is not associated with improvement in colonoscopy quality metrics.

Disclosure: Mayur Brahmania: Roche (Consultant, investigator, speaker), Merck (Investigator, speaker), AbbVie (Speaker), Eisai (Consultant, investigator)

P1202 WITHDRAWN

P1203

EFFECT OF A RISK STRATIFICATION SCORE ON IMPROVING SENSITIVITY FOR ADVANCED COLORECTAL NEOPLASIA IN COLORECTAL CANCER SCREENING

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Introduction: Fecal immunochemical test (FIT) is widely used in colorectal cancer (CRC) screening; however, the screening sensitivity of FIT for advanced colorectal neoplasia (ACN) is reportedly relatively low, and interval cancer remains an issue. Although the diagnostic accuracy of FIT can be adjusted by changing the cut-off level of quantitative FIT and/or using multiple FIT samples per screening, the effects of these adjustments are limited. In this context, a risk score comprising easily collectable factors pertaining to individual characteristics that stratifies screened individuals by ACN risk may be useful, especially when used with FIT.^{1,2} However, the diagnostic accuracy of a risk score with FIT is not fully understood.

Aims & Methods: This study aimed to elucidate the diagnostic accuracy of the combination of the risk score and FIT for ACN and compare it with that of 1-day and 2-day FIT alone with different cut-off levels by using

high-quality colonoscopy results as a reference. This cross-sectional study used data from a prospective cohort in a Japanese island, Izu Oshima. Inhabitants aged 40-79 years without uncontrollable complications were recruited, and underwent both 2-day FIT and colonoscopy between 2015 and 2017. Individuals with a history of colorectal surgery or colonoscopic treatment were excluded. An 8-point risk score recently developed by modifying the Asia-Pacific Colorectal Screening score was assessed.³ The score was based on the following factors: sex (male: 1 point, female: 0), age (years; 40-49: 0, 50-59: 2, 60-69: 3, ≥ 70 : 3.5), CRC family history (presence of ≥ 2 first-degree relatives with CRC: 2, others: 0), body mass index (kg/m^2 ; ≤ 22.5 : 0, > 22.5 : 0.5), and smoking history (pack-years; ≤ 18.5 : 0, > 18.5 : 1).

Results: Overall, 1,191 individuals [518 (43.5%) males] with a median age of 63.0 years were included. The proportions of those with CRC and ACN were 0.8% and 9.4%, respectively. The sensitivity and specificity for ACN were 17.9-24.1% and 95.0-97.6%, respectively, for 1-day FIT, and 22.3-33.9% and 91.8-96.5%, respectively, for 2-day FIT (cut-off 50-200 ng Hb/mL for both). The risk score had a c-statistic for ACN of 0.66 (95% confidence interval, 0.61-0.72), and ACN was noted in 3.8%, 9.3%, and 17.7% of individuals with low (< 3), intermediate (≥ 3 to < 5), and high (≥ 5) risk scores, respectively. The combination of the risk score and 1-day FIT (cut-off 100 ng Hb/mL), in which individuals with high risk scores underwent colonoscopy first and individuals with low/intermediate risk scores underwent FIT first followed by colonoscopy for FIT-positive subjects, had a sensitivity and specificity of 49.1% and 80.0% for ACN, respectively. The combination of the risk score and 2-day FIT (cut-off 100 ng Hb/mL) had a sensitivity and specificity of 54.5% and 78.2% for ACN, respectively. The sensitivities for right-sided ACN of 1-day FIT (50-200 ng Hb/mL), 2-day FIT (50-200 ng Hb/mL), the risk score with 1-day FIT (100 ng Hb/mL), and the risk score with 2-day FIT (100 ng Hb/mL) were 4.9-12.2%, 7.3-22.0%, 43.9%, and 46.3%, respectively.

Conclusion: The risk score had a strong effect on increasing the screening sensitivity for ACN, particularly right-sided ACN. Although the specificity decreased with the score, the combination of the score and FIT still maintained the relatively high specificity. The additional use of the score with FIT is believed to provide useful noninvasive screening options with high sensitivity, thereby allowing to select a more suitable screening method according to the colonoscopy resource capacity.

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Disclosure: Nothing to disclose

P1204

COMPUTER-AIDED DIAGNOSIS FOR INVASIVE COLORECTAL CANCER: A VALIDATION STUDY DESIGNED TO OBTAIN REGULATORY APPROVAL

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Introduction: Endoscopic diagnosis for large ($> 20\text{mm}$) colorectal lesions is considered important because some of them are invasive cancers harboring the risk of lymph node metastasis, which should be removed surgically rather than endoscopically. We developed an artificial intelligence (AI) system for endocytoscopy (H290ECI, Olympus Corp.; 520-fold contact endomicroscopy) that allowed real-time identification of invasive cancer during colonoscopy [1].

The present study is a bench-mark test to validate the performance of this AI system. It is also a study designed to obtain regulatory approval, which was monitored by the Pharmaceuticals and Medical Devices Agency, a regulatory body in Japan.

Aims & Methods: The AI system (EB-02, prototype from Cybernet Corp. Tokyo) was developed by collecting colonoscopic pictures from six Japanese institutions as learning material between January 2016 and September 2019. The system output predicted pathology of the targeted lesion as either invasive cancer, adenoma, or non-neoplastic with a probability of its prediction. A validation test was produced employing 500 endocytoscopic images from 50 large colorectal lesions ($\geq 20\text{ mm}$) taken in a university hospital. There was no overlap between the learning and validation material. The validation test was assessed by the AI system under the controlled environment. Primary outcome measure was the specificity in identifying invasive cancer.

Results: A total of 60,899 endocytoscopic images were used for machine learning. The 50 lesions used for the validation consisted of 30 invasive cancers (8 T1 cancers and 22 T2-4 cancers), 15 adenomas, and 5 non-neoplastic lesions. 84% (418/500, 95% confidence interval [CI]: 80%-87%) of the images for these lesions were analyzable via the AI system, while remaining were recognized as non-analyzable due to their poor image quality. Among the analyzable 418 images, the AI system correctly predicted the pathology of 384 images, resulting in an overall accuracy of 92% (95% CI: 89%-94%). Its sensitivity and specificity in identifying invasive cancer was 92% (212/231, 95%CI: 88%-95%) and 97% (182/187, 95%CI: 94%-99%).

Conclusion: The newly developed AI system designed for endocytoscopy allowed reliable performance in the prediction of invasive colorectal cancer. (Clinical trial registry. No.UMIN000037977. Acknowledgement: This study was supported by Japan Agency for Medical Research and Development).

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P1205

EARLY REMODELING OF THE COLONIC MUCOSA AFTER ALLOGENEIC HEMATOPOIETIC STEM CELLS TRANSPLANTATION: AN OPEN-LABEL CONTROLLED PILOT STUDY ON 19 PATIENTS

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Introduction: Graft-versus-host disease (GVHD), in particular acute digestive GVHD (aDGVHD), is a severe and frequent complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT). Prophylactic treatment carries a significant risk of drug toxicity and infections and therefore has to be tailored to the estimated risk of GVHD. It is thus necessary to identify potential predictive factors of GVHD. Intestinal epithelial barrier loss seems to play a pivotal role in the initiation of GVHD.

Aims & Methods: This pilot study aimed i) to determine whether an early remodeling of the colonic mucosa occurred after allo-HSCT and ii) to identify potential predictive mucosal markers of aDGVHD after allo-HSCT. Between day 21 and day 28 after the allo-HSCT, 19 allo-HSCT patients were included; there was a majority of males (63%) and the mean age was 61.3 years old (38-69). Ten (53%) patients were treated for an acute leukemia, 7 (37%) for a non-Hodgkin leukemia and 2 (10%) for an aplastic anemia. All patients had a rectosigmoidoscopy with probe-based confocal endomicroscopy (pCLE) recording and biopsies at 30 cm from the anal margin.

A 5-minutes pCLE recording of the colonic mucosa was performed using a dedicated CLE system, composed of a portable laser station and an endoscopic probe, after intravenous injection of 5 mL of a 10% fluorescein sodium solution. Seven subjects who underwent a colonoscopy for screening or surveillance of polyps/cancer and had a pCLE examination performed for research purposes served as a control group in the pCLE part of our study and 5 subjects who underwent surgery for colon cancer served as control for assessment of cytokine levels in the supernatants of mucosal explants, taken at distance from the tumor. Morphological (pCLE), functional (intestinal permeability) and inflammatory parameters (cytokine multiplex immunoassay) were assessed.

Results: Among allo-HSCT patients, 11 patients developed GVHD and 6 of them developed aDGVHD. Morphological and functional changes of the colonic mucosa occurred after allo-HSCT. Indeed, the median perimeter of colonic crypts was significantly increased in allo-HSCT patients ($676 \pm 176 \mu\text{m}$) compared to controls ($483 \pm 46 \mu\text{m}$) and crypts median sphericity and roundness were significantly decreased in allo-HSCT patients ($41 \pm 10\%$ and $47 \pm 15\%$, respectively) compared to the control group ($62 \pm 9\%$ and $60 \pm 4\%$, respectively). In addition, IL-6, IL-33 and IL-15 levels were significantly increased in allo-HSCT patients compared to controls, in the supernatants of 24h-explant cultures of colonic biopsies. Finally, there was no difference in pCLE, intestinal permeability and inflammatory cytokines between patients who developed aDGVHD and those who did not.

Conclusion: This pilot study of mucosal remodeling after allo-HSCT identified morphological and immunological changes, which are in particular related to mucosal alteration occurring after conditioning. However,

analysis of pCLE parameters, intestinal permeability and cytokines did not identify predictive markers of GVHD. Future studies following larger cohort based on the analysis of these parameters are warranted.

Disclosure: Nothing to disclose

P1206

IMPACT OF THE IMMUNOHISTOCHEMICAL LYMPHOVASCULAR EVALUATION IN JUDGEMENT OF CURABILITY FOR PATIENTS WITH COLORECTAL T1 CARCINOMA AFTER ESD - A MULTICENTER PROSPECTIVE STUDY

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Introduction: This study is to clarify the usefulness of immunohistochemical lymphovascular evaluation as an indicator for additional surgery after endoscopic submucosal dissection (ESD) for patients with submucosal invasive (T1) colorectal carcinoma (CRC).

Aims & Methods: We prospectively investigated 420 consecutive T1 CRCs after ESD at 3 hospitals in Japan between January 2012 and December 2017. (Evaluation 1) Prognosis of 247 cases considered for additional surgery after ESD. (Evaluation 2) Pathological risk factors for lymph node (LN) metastasis of the 215 lesions which underwent an additional surgery after ESD, including immunohistochemical lymphovascular evaluation.

Results: (Evaluation 1) The number of cases which underwent additional surgery after ESD were 76% (187/247). The reasons of cases without additional surgery were as follows: the other risk factors were negative except submucosal invasion depth: 32 (53%), elderly cases: 16 (27%), refusing surgery: 27 (45%), severe complication: 4 (7%) (Overlap exists.). The recurrence occurred in 6 cases, and the 4 cases were those with additional surgery. The lesions which have no risk factor except submucosal invasion depth did not show recurrence. (Evaluation 2) The number of LN metastasis were 21 (10%). Among 16 cases with additional surgery due to the risk factor of lymphovascular invasion alone, there were 3 (19%) cases with LN metastasis. The histological characteristic of lesion with LN metastasis were as follows, unfavorable histology: 1 (5%), submucosal invasion depth $\geq 1000 \mu\text{m}$: 19 (86%), lymphatic invasion positive: 18 (82%), venous invasion positive: 12 (55%), high grade budding: 13 (59%), existence of poorly differentiated component: 12 (55%), poorly or mucinous differentiation at the depth invasive portion: 17 (77%), infiltrative growth b/c: 17 (77%), incompletely disrupted with deformity or completely disrupted of muscularis mucosa: 22 (100%) and invasion width $\geq 2500 \mu\text{m}$ were 20 (91%) (Overlap exists.). Significant risk factors for LN metastasis in univariate analysis were lymphatic invasion positive, high grade budding, the poorly differentiated component, poorly or mucinous differentiation at the depth invasive portion and invasion width $\geq 2500 \mu\text{m}$ ($P < 0.05$). Significant predictive factors for LN metastasis in multivariate analysis with logistic regression were lymphatic invasion positive (OR 4.8, 95% CI 1.3-17.5, $P = 0.0187$).

Conclusion: Additional surgery should be considered after ESD based on both risk factors for LN metastasis and the background of patients. Immunohistochemical lymphatic evaluation could be the most reliable predictive factor for LN metastasis.

Disclosure: Nothing to disclose

P1207

EFFECT OF IMPLEMENTING A REGIONAL REFERRAL NETWORK ON SURGICAL REFERRAL RATE OF BENIGN POLYPS FOUND DURING A COLORECTAL CANCER SCREENING PROGRAM: A POPULATION-BASED STUDY

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Introduction: Organized screening for colorectal cancer (CRC) by fecal occult blood testing followed by colonoscopy reduce CRC incidence and mortality. Increasingly, large pre-neoplastic lesions are discovered through fecal immunochemical test (FIT) and endoscopic resection is the current reference method to resect them.

Although a significant number of colorectal surgeries are still reported for these lesions.

Aims & Methods: Population-based study in 2012, 2016 and 2017, analyzing the evolution of surgical management of benign polyps over 2 centimeters discovered in the context of organized CRC screening after the implementation of a regional referral network for the management of superficial colorectal lesions.

We studied the years 2012, 2016 and 2017 in order to compare the performances of the *Hemoccult II* test and the FIT implemented in 2015, as well as the possibilities for the management of benign colorectal lesions, since from 2015 a referral network with expert endoscopists was set up in the academic hospital of our administrative area.

The primary outcome was to study the evolution of surgical management for benign lesions before and after the development of an expert network in interventional endoscopy.

Secondary outcomes were to look at the surgical management rate by type of establishments, assess risk factors for surgical management of benign polyps, study the results of surgical and endoscopic management of polyps ≥ 2 cm, and to compare the performances of the guaiac test and the FIT.

Results: Over the study period, 1571 patients had a colonoscopy following a positive test, 981 colonoscopies revealed at least one lesion.

Concerning the primary outcome, the surgical management rate for benign lesions decreased significantly from 14.6% in 2012 to 7.5% in 2016 and 5% in 2017 ($p=0.016$).

Concerning the secondary outcomes, surgical management of benign lesions was significantly higher in the private sector (10% compared to 2.8%, $p=0.001$) but tends to decrease (2012: 21.8%, 2016: 9.89%, 2017: 5.96%, $p=0.004$).

After uni and multivariate analysis we identified risk factors for the surgical management of benign lesions: year 2012 (OR:3.35, $p=0.022$), high-grade dysplasia (OR:2.49, $p=0.04$), *in situ* carcinoma (OR:5, $p=0.003$), size ≥ 20 mm (OR:17.39, $p<0.0001$), private sector (OR:6.6, $p=0.0002$).

Size or an error in characterization represented the reason for direct surgery in 75% of cases.

Morbidity at one month for benign lesions ≥ 20 mm was 20.4% (versus 6% with endoscopy, $p=0.044$) and the cost was 6 times higher with surgery (7198 euros versus 1129 euros, $p<0.0001$).

The adenoma detection rate (ADR) was 57%, lower for the 2012 tests (*Hemoccult II*) at 40% compared to 62% and 57.5% in 2016 and 2017 (FIT) ($p<0.0001$).

Conclusion: This study shows a direct effect of the implementation of a regional network on the number of surgical managements for superficial colorectal lesions when an effective mass screening test is available.

Since the problems related to the size and characterization of lesions are the two main risk factors for direct surgery, improvement will involve artificial intelligence and implementation of technological tools allowing rapid expert advice.

Our results concur with known data concerning the morbidity of surgery for benign lesions with 20.4% morbidity at one month and a higher cost (6 times higher).

Finally, our study also concurs with the literature about the superiority of FIT over the Guaiac test with a significantly higher ADR.

Disclosure: Nothing to disclose

P1208

PROPHYLACTIC CLIPPING AFTER NON-PEDUNCULATED COLORECTAL POLYP RESECTION: SYSTEMATIC REVIEW AND INDIVIDUAL PATIENT DATA META-ANALYSIS

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Introduction: Non-pedunculated colorectal polyps are removed endoscopically with hot- or cold-snare polypectomy or by endoscopic mucosal resection (EMR) to prevent neoplastic progression. Delayed bleeding is the most common complication after polyp resection. Prophylactic clipping of the resection defect is suggested to reduce the incidence of delayed bleeding. Although evidence for the benefit of prophylactic clip closure for proximal colon lesions is growing, there is a lack of data on clip closure for patients on antithrombotics.

We aimed to determine the efficacy of prophylactic clipping on delayed bleeding after colorectal polyp resection, and the contribution of routine antithrombotic use in triaging patients for prophylactic clipping.

Aims & Methods: We performed a systematic review with an Individual Patient Data Meta-Analysis. Studies that included non-pedunculated colorectal polyp resections of all sizes with prophylactic clipping and controls were selected from PubMed, Embase, Web of Science and Cochrane database (last search: April 2020).

Authors of eligible studies were invited to share the original study data. Risk of bias was assessed using the Cochrane tool for randomized trials and the Newcastle-Ottawa score for observational studies. The primary outcome was the effect of prophylactic clipping in reducing clinically sig-

nificant delayed bleeding within 30 days. Secondary outcomes were the effect of antithrombotics on delayed bleeding rate and prophylactic clipping efficacy. Multivariable analysis was used to determine the efficacy of prophylactic clipping with correction for potential confounders, such as polyp size, proximal polyp location and antithrombotic use.

Results: Individual patient data of 8949 resected polyps from 13 original studies (3 RCT's, 8 retrospective and 2 prospective studies; response rate 28.9%, $I^2=85\%$) were included. In 3179 (35.5%) polyps prophylactic clipping was applied. Periprocedural antithrombotics were managed according to local protocol. Delayed bleeding occurred in 260 (2.9%) polyps in 223 patients.

Antithrombotics increased the overall risk of delayed bleeding two-fold (OR 2.02, 95% CI 1.55 - 2.63, $p<0.01$). Other risk factors for both delayed bleeding and prophylactic clip use were polyp size and proximal location. Prophylactic clipping did not prevent delayed bleeding in adjusted analysis (OR 1.14, 95% CI 0.84 - 1.52, $p=0.43$).

However, in cases in which complete closure was achieved, prophylactic clipping significantly reduced delayed bleeding in proximal polyps ≥ 20 mm (N=1916, OR 0.40, 95% CI 0.17 - 0.95, $p=0.04$) and in any polyp in patients on antithrombotics (N=1717, OR 0.23, 95% CI 0.07 - 0.77, $p=0.02$) (See Table 1). This effect seemed strongest in patients on vitamin K antagonists. Clipping did not significantly reduce delayed bleeding in patients with distal polyps ≥ 20 mm who were on antithrombotics (N=180, OR 0.49, 95% CI 0.06 - 4.22, $p=0.52$).

Conclusion: Prophylactic clipping after resection of colorectal polyps of any size did not reduce delayed bleeding. However, complete clip closure decreased the risk of delayed bleeding for non-pedunculated colorectal polyps ≥ 20 mm in the proximal colon, and for polyps of any size among patients on antithrombotics. Further studies are needed to investigate whether improvement of clip closure techniques reduce bleeding risk in patients with an increased risk of delayed bleeding.

Disclosure: This IPDMA was registered in the PROSPERO database under registration number CRD42020104317. No funding was obtained for this project.

P1209

EFFECTIVENESS AND SAFETY OF NER1006 VERSUS STANDARD BOWEL PREPARATIONS: A META-ANALYSIS OF THREE RANDOMISED PHASE-3 CLINICAL TRIALS

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Introduction: The effectiveness of bowel cleansing is essential for a quality colonoscopy, especially in the setting of colorectal cancer screening. Despite this, suboptimal bowel preparation is still observed in 25% of procedures. Recently, a 1L PEG-based preparation for colonoscopy (NER1006) has been introduced to improve the patient's experience in colonoscopy.

Aims & Methods: We conducted a meta-analysis of randomized controlled trials (RCTs) to explore cleansing success, adenoma detection rate (ADR), and safety profile of NER1006 versus standard preparations. PubMed/Medline and Embase were systematically searched through January 2020 by two independent reviewers for phase-3 RCTs comparing the effectiveness of NER1006 versus standard preparations.

Results: Three RCTs (1879 participants) met the inclusion criteria and were included in the meta-analysis. The analysis showed a significantly higher cleansing success for NER1006 compared standard preparation both using the Harefield Cleansing Scale (HCS) (OR=1.28; 95% CI 1.00-1.62; $p=0.047$, $I^2=0\%$, 1879 participants) and the Boston Bowel Preparation Scale (BBPS) (OR=1.43; 95% CI 1.13-1.80; $p=0.003$, $I^2=1.0\%$, 1879 participants), as well as a significantly greater high-quality cleansing of the right colon when assessed with the HCS (OR=2.13; 95% CI 1.16-3.94; $p=0.015$, $I^2=76.0\%$, 1879 participants). The pooled estimate of the NER1006 effect on ADR showed no significant difference on overall ADR (OR=1.03; 95% CI 0.84-1.27; $p=0.769$, $I^2=0\%$, 1879 participants), and a slightly higher, although not significant, ADR of the right colon (OR=1.19; 95% CI 0.73-1.92; $p=0.485$, $I^2=53\%$, 1879 participants).

When considering the impact of NER1006 on mild to moderate treatment-emergent adverse events (TEAEs), we observed a significant pooled estimate of number of TEAEs (OR=2.31; 95% CI 1.82-2.94; $p<0.001$, $I^2=0\%$, 1797 participants) and of patients with TEAEs (OR 1.79; 95% CI 1.32-2.44; $p<0.001$, $I^2=0\%$, 1797 participants). No serious adverse event occurred neither in NER1006 and standard preparation group.

Conclusion: When compared to traditional preparations, NER1006 showed a better overall cleansing of the colon as well as a greater high-quality cleansing of the right colon, with a comparable ADR. A higher incidence of mild to moderate TEAEs was observed for NER1006, in the absence of serious adverse events.

Disclosure: Nothing to disclose

P1210

VIRTUAL CHROMOENDOSCOPY COMBINED WITH ENDOCUFF FOR SCREENING COLONOSCOPY IS FEASIBLE ACHIEVING A HIGH ADENOMA DETECTION RATE: RESULTS OF A PROSPECTIVE SINGLE CENTER STUDY

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Introduction: The adenoma detection rate (ADR) is inversely associated with the risk for interval colorectal cancer (CRC). An ADR $>25\%$ is therefore crucial for the effectiveness of CRC surveillance programs, and tools to improve the ADR especially in less-experienced endoscopists are needed. Recent findings suggest that add-on devices such as Endocuff (EC) increase the ADR. Additionally, a recent meta-analysis indicates a significantly increased ADR using narrow band imaging (NBI), but only in cases with excellent bowel preparation. We aimed to evaluate the ADR in patients undergoing screening colonoscopy using the combination of EC and NBI.

Aims & Methods: We prospectively analyzed all patients undergoing screening colonoscopy using combined EC and NBI between September 2019 and March 2020 at the Kantonsspital St. Gallen, Switzerland. Excluded were patients with a Boston bowel preparation score (BBPS) <8 and withdrawal time <6 minutes. Patients underwent colonic lavage with a split dose of macrogol 3350 (Moviprep; Norgine, Amsterdam, the Netherlands) over 2 days. Colonoscopies (PCF-H190, CF-HQ 190 AL, Olympus, Tokyo, Japan) were performed by one experienced board-certified gastroenterologist (>5000 colonoscopies) and two less experienced gastroenterologists (<1000 colonoscopies). ADR and SSA detection rate were determined. Residual pollution in NBI of each bowel segment (Colon ascendens, transversum and left colon) was assessed by each endoscopist using an additional modified NBI-BBPS score (1 point per segment if no residual pollution, ranging from 0-3).

Results: 105 patients (median age 62 years, 54% male) with a median modified NBI-BBPS of 3 (1-3) were included. Overall ADR and detection rate for sessile serrated adenoma (SSA) were 57% and 11%, respectively. ADR and SSA detection rate did not significantly differ between experienced and less experienced endoscopists (59% vs. 54%, $p=0.377$, and 15.3% vs 4.3%, $p=0.065$). A higher modified NBI-BBPS was not associated with a higher likelihood of adenoma detection (OR 1.219, 95%CI 0.331-4.485, $p=0.766$).

Conclusion: Screening colonoscopy using EC in combination with NBI is feasible achieving an excellent ADR of 57%. In particular less experienced endoscopists seem to benefit from the combination of EC and NBI resulting in an ADR comparable with that of an experienced gastroenterologist.

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Disclosure: Nothing to disclose

P1211

MICROSCOPIC COLITIS - MYTH OR TRUTH?

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Introduction: In a recent study carried out at our service, it was found that the performance of random biopsies for the investigation of microscopic colitis is lower than recommended.

Thus, the aim of this study was to assess the prevalence and distribution of microscopic colitis and, whether the performance of biopsies can influence diagnostic performance.

Aims & Methods: It was conducted a retrospective study that included complete colonoscopies, due to chronic non-bloody diarrhea, and biopsies for microscopic colitis investigation, between 2013 and 2019.

Results: Were included 107 complete colonoscopies and was observed a prevalence of 12.1% of microscopic colitis ($n = 13$; 69.2% men, mean age 58.69 ± 14.7 years). No patient had celiac disease or was a smoker, 30.5% had diabetes, 15.4% had weight loss and 30.8% had abdominal pain. Most patients had biopsies in 2 bottles (left and right) or 4 bottles (4 segments) (38.5% and 30.8%, respectively).

All patients had microscopic lymphocytic colitis, which was diffusely distributed in 76.9% of cases. Sigmoid and transverse were not affected in 3 patients (23.1%), with no differences in the number of fragments that could justified it. On average, each bottle had 2.8 fragments (range 1-8).

It was found that males are less likely to have microscopic colitis ($p = 0.009$; OR 0.170 [CI 0.048-0.6]). There was no association with abdominal pain, diabetes or weight loss ($p > 0.05$, $n = 107$). Diagnostic performance was not associated with performance, number of biopsy fragments or physician ($p > 0.05$).

Conclusion: In this population, the prevalence of microscopic colitis is not lower than that described in the literature. (1) Although it may be underestimated once the biopsies are not performed in all colonoscopies executed due to diarrhea. In all patients ascending colon was affected, but

in 23.1% microscopic colitis was not extended to more distal segments. Thus, biopsies of the right colon should always be performed, and the left colon may eventually be excluded.

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Disclosure: Nothing to disclose

P1212

OBJECTIVE MEASUREMENT OF STRESS LEVEL REDUCTION BY INDIVIDUALLY CHOSEN MUSIC DURING COLONOSCOPY - RESULTS FROM THE COLORELAXTONE STUDY

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Introduction: Colonoscopy as standard procedure in endoscopy is often perceived as uncomfortable for patients. Patient's anxiety is therefore a significant issue, which often lead to avoidance of participation of relevant examinations as CRC-screening. Non-pharmacological anxiety management interventions such as music might contribute to relaxation in the phase prior and during endoscopy. Although music's anxiolytic effects have been reported previously, no objective measurement of stress level reduction has been reported yet. Focus of this study was to evaluate the objective measurement of the state of relaxation in patients undergoing colonoscopy.

Aims & Methods: Prospective, pilot study performed at one endoscopic high-volume center. Standard colonoscopy was performed in control group. Interventional group received additionally self-chosen music over earphones. Facial Electromyography (fEMG) activity was obtained. Clinician Satisfaction with Sedation Instrument (CSSI) and Patients Satisfaction with Sedation Instrument (PSSI) was answered by colonoscopists and patients respectively. Overall satisfaction with music accompanied colonoscopy was obtained if applicable.

Results: Mean difference measured by fEMG via *musculus zygomaticus major* indicated a significantly lower stress level in the music group ($7.700(\pm 5.560)$ μV vs. $4.820(\pm 3.330)$ μV ; $p=.001$). Clinician satisfaction was significantly higher with patients listening to music ($82.69(\pm 15.04)$ vs. $87.3(\pm 15.02)$ pts.; $p=.001$).

Conclusion: We conclude that self-chosen music contributes objectively to a reduced stress level for patients and therefore subjectively perceived satisfaction for endoscopists. Therefore, music should be considered as a non-pharmacological treatment method of distress reduction especially in the beginning of endoscopic procedures.

Disclosure: Nothing to disclose

P1213

USE OF ARTIFICIAL INTELLIGENCE TO PREVENT SEVERE PERFORATION DURING ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASM: A PROOF-OF-CONCEPT STUDY

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Introduction: Endoscopic submucosal dissection (ESD) has been catching considerable attention as less invasive treatment for large colorectal neoplasms. However, it is not widely spread due to its high complication rate; perforation occurs in approximately 5%-20%, some of which require surgical intervention. To change this unfavorable situation, we developed artificial intelligence (AI) system which can prevent overlooking perforation during ESD.

Aims & Methods: We retrospectively collected 50 ESD videos from June 2014 to March 2017 at Showa University Northern Yokohama Hospital. One endoscopist who has experienced in colorectal ESD annotated all the video frames (N=100,951) as either perforation frames or non-perforation frames. All the annotated image frames were randomly divided into two groups:

- 1) learning data for machine learning (20,903 perforation frames and 58,383 non-perforation frames) and;
- 2) test data for evaluation of the model (6,034 perforation frames and 15,631 non-perforation frames).

AlexNet, a convolutional neural network model, was used to construct the prediction model to identify perforation and its performance was assessed using the test data.

Results: We constructed three models having different kinds of networks with three, four, and five convolutional layers, respectively. Perforation status was identified with sensitivity, specificity, and accuracy of 88.7%, 70.7%, and 75.7% respectively in the three-layer convolutional model, and 71.8%, 77.2%, and 75.7%, respectively in the four-layer convolutional model, and 81.4%, 70.5%, and 73.6%, respectively in five-layer convolutional model.

Conclusion: The three-layer model worked best in terms of sensitivity and accuracy. Our proposed AI system has the potential to accurately identify the micro-perforation at an early stage, possibly contributing to reduction of surgical intervention.

Disclosure: Nothing to disclose

P1214

DOUBLE CLIP AND RUBBER BAND TRACTION METHOD FOR COLONIC ENDOSCOPIC SUBMUCOSAL DISSECTION (DCT-ESD) USING A SMALL-CALIBER-TIP TRANSPARENT HOOD (ST HOOD)

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Introduction: In recent years, the effectiveness of various traction methods for colonic endoscopic submucosal dissection (ESD) has been demonstrated, and ESD with double clip and rubber band traction (DCT-ESD) is a method using an orthodontic rubber band. The rubber band is easy to

prepare in advance and can be added during the procedure through the instrument channel. In our hospital, we use a small-caliber-tip transparent hood (ST hood) for colorectal ESD and perform conventional ESD (combination with a needle-type tip and ST hood).

Aims & Methods: We retrospectively reviewed all patients who underwent colorectal ESD at our hospital between April 2019 and March 2020. We initiated colorectal ESD with the conventional method using a needle-type tip and ST hood. When the dissection became difficult, we made a circumferential incision and switched to DCT-ESD. Cases of NET (neuroendocrine tumor), SMT (submucosal tumor), and cases located on the rectum were excluded. We divided the patients into two groups: those who underwent DCT-ESD and those who did not undergo DCT-ESD. The primary endpoint was the rate of en bloc resection, complete resection, and complications. Complications were defined as perforation and delayed bleeding. The secondary endpoint was procedure speed [area (mm²) / resection time (min)]. [Area(mm²)]= (smaller diameter (mm)/2) × (larger diameter (mm)/2) × π.

Results: A total of fifty-nine patients were enrolled; 6 patients were assigned to the group that underwent DCT-ESD and 30 patients were assigned to the group that did not undergo DCT-ESD. En bloc resection rate was 100% in both groups. Complete resection rate was 100% (6/6) in the group that underwent DCT-ESD and 90% (27/30) in the group that did not undergo DCT-ESD. There was no significant difference in the rate of complications between the two groups (p=0.31): the rate of perforation was 16.7% (1/6) in the group that underwent DCT-ESD and 3.3% (1/30) in the group that did not undergo DCT-ESD. No delayed bleeding occurred. There was no salvage surgery required to treat the complications. There was no significant difference in the procedure speed between two groups (p=0.09): the median procedure time was 9.52 mm²/min (SD: 3.50) in the group that underwent DCT-ESD and 13.09 mm²/min (SD: 7.52) in the group that did not undergo DCT-ESD. This study did not show a significant difference in the procedure speed between the cases that underwent DCT-ESD and those that did not. The reason for this result might be that the group that underwent DCT-ESD included many cases that were difficult to keep visualize the submucosal layer and under poor maneuverability conditions. The limitations of this study were small sample size and retrospective study conducted in single center, so this result of the procedure speed is expected to improve with experience in the future.

	the group that underwent DCT-ESD [n/total (%)]	the group that did not undergo DCT-ESD [n/total (%)]	P value
En bloc resection	6/6 (100)	30/30 (100)	-
Complete resection	6/6 (100)	27/30 (90)	-
Complications	1/6 (16.7)	1/30 (3.3)	0.31
Procedure speed (mm ² /min) [mean(SD)]	9.52 (3.50)	13.09 (7.52)	0.09

[A comparison of outcomes for each group]

Conclusion: In cases where it was difficult to visualize the submucosal layer during conventional ESD using an ST hood, switching to the DCT-ESD made it easier to dissect the submucosal layer. DCT-ESD appears to be safe and useful for en bloc resection and complete resection.

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Disclosure: Nothing to disclose

P1215

THE EFFECT OF THE ENDOSCOPIC ADJUNCT DEVICE ENDOCUFF/ENDOCUFF VISION ON QUALITY STANDARDS IN LOWER GI ENDOSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Colonoscopy is the gold standard investigation for lower gastrointestinal symptoms with adenoma detection rate (ADR) considered the most important benchmark for evaluating the quality and completeness of mucosal visualisation. A number of devices to improve ADR have been investigated.

This systematic review and meta-analysis assessed the effects of Endocuff or Endocuff Vision assisted colonoscopy (EAC) on ADR and other clinical related outcomes compared with standard colonoscopy (SC).

Aims & Methods: Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were adhered to. Searches were conducted of Medline, Embase, Web of Science, Scopus and the Cochrane Central Register to 08/02/2019. Full text randomised controlled studies and crossover studies of >50 patients comparing Endocuff (EC) or Endocuff Vision (EV) with SC were eligible. Studies of polyposis syndromes or inflammatory bowel disease surveillance were excluded.

Data were abstracted by two independent reviewers. The primary outcome was ADR. Secondary outcomes included the polyp variables mean adenomas per procedure (MAP), polyp detection rate (PDR), mean polyps per procedure (MPP), and procedure variables procedure time, withdrawal time and caecal intubation time, caecal intubation rate and complication rate. Meta-analysis, using inverse variance and random effects models, was used to compute pooled estimates of outcomes (relative risk (RR) with 95% confidence interval (CI) for dichotomous outcomes, mean difference with 95% CI for continuous outcomes). Study quality was assessed with the Cochrane risk of bias tool.

Results: Of the 661 articles reviewed, 8 randomised controlled trials and 2 randomised crossover studies involving 6238 patients were eligible; 8 studies evaluated EC and 2 EV. All studies included mixed populations by indication (screening, surveillance, symptoms) and endoscopist experience (expert or mixed expert and trainee/fellow). EAC significantly increased ADR compared to SC (41.5% vs 34.4%; RR 1.21 (1.10-1.34); 10 studies, $I^2 = 59\%$), MAP (1.20 vs 1.01; mean difference 0.19 (0.02-0.37); 9 studies, $I^2 = 87\%$), PDR (60.1% vs 51.3%; RR 1.25 (1.09-1.43); 7 studies, $I^2 = 88\%$) and MPP (1.53 vs 1.15; mean difference 0.38 (0.12-0.30); 5 studies, $I^2 = 86\%$) were significantly higher compared to SC.

There were no significant differences in advanced adenoma and sessile serrated lesion detection rates. No difference was seen in ADR by colonic segment (left vs right), but polyp detection was significantly increased in the sigmoid [RR 1.96 (1.54-2.50)], transverse colon [RR 1.61 (1.02-2.54)] and caecum [RR 1.80 (1.19-2.72)].

There were no significant differences between EAC and SC in procedure variables. Complications related to EAC were uncommon. Cuff exchange rates ranged from 1.3-7.0% in 6 studies. All 10 studies were rated low risk of bias.

Conclusion: Our results indicate that Endocuff and Endocuff Vision are associated with increased ADR, MAP, PDR and MPP compared with standard colonoscopy, with no detrimental effects on procedure measures. Cost-effectiveness analyses are lacking but would be valuable to inform practice recommendations.

Disclosure: Nothing to disclose

P1216

ESD CURRICULUM IN FRANCE : A COMPARATIVE STUDY OF LEARNING CURVES IN 3 FRENCH CENTERS WITH DIFFERENT TRAINING METHODS

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Introduction: Endoscopic submucosal dissection (ESD) is now an essential technique for the resection of superficial neoplasm of the gastrointestinal tract. Its development in Europe remains limited compared as our Japanese colleagues. The European Society of Gastrointestinal Endoscopy (ESGE) recently published a position paper on the curriculum for ESD training in Europe.

The aim of our study was to compare the learning curve of 3 french tertiary endoscopic centers with 3 different training methods.

Aims & Methods: 450 patients were included to analyse learning curves of the 150th first cases of 3 centers: one center with two operators trained independently on animal model only (center A, from march 2012 to December 2017), a center with a single operator trained on animal model with exchanges with french experts (center B, from September 2016 to April 2019) and a center with a single operator with a one-year fellowship in a european expert center and animal model (center C, from June 2016 to September 2019). Data were prospectively collected.

The primary endpoint was the curative resection rate. Secondary endpoints were the monobloc resection rate, the histological complete resection rate, the size of lesions, the speed of resection, the complication rate and the location.

Results: Respectively, for centers A, B and C, monobloc resection rates were 96,0%, 91,3% and 94%. The histological complete resection rate were 79,3%, 77,3% and 81,8% and the curative resection rates were 73,3%, 73,4 and 73,4% without any significant difference.

Respective perforation rates were 8,0% (A), 2,7% (B) and 6,7% (C).

All centers experienced significantly increased curative resection rate after the 75th case (77,8% vs 68,9%, $p=0,034$). The size of lesions increased with experience (1507mm² before 75 cases vs 1904mm² after 75 cases, $p< 0,0001$) whereas the length of procedures decreased (126,3min vs 90,7min, $p=0,036$).

The average time to perform 30 ESD was 247 days, decreasing over time.

The speed of procedure was significantly faster in the centers B and C than in center A, respectively 22,8mm²/min, 19,49mm²/min and 13,52 mm²/min ($p< 0,0001$). The speed increased with the number of procedures. (

The location of the lesions was distributed differently according to the center and center B et C as more recently trained operators, early experienced colonic ESD comparatively to center A (respectively 57,3% and 38,0% vs 19,3%, $p< 0,0001$). In the same way, centers B and C used more frequently and from the start of their experience a countertraction system with clip and rubber band than center A (63,3% and 67,7% and 25,3 of procedures, $p< 0,0001$).

Conclusion: Training in endoscopic submucosal dissection seems to be possible in Europe with curative resections rates closes to those published in Japanese studies. Performance and outcomes increase with the number of procedures and it is necessary to obtain sufficient recruitment of patients to achieve satisfying curative resection rates. Several training methods exist and our study did not show any difference on the resection rates according to the training method. Nevertheless, there seems to be a significant progression in terms of speed of procedure among centers using from the start of their experience a countertraction method. Despite less complete training than recently recommended by ESGE, the results of these 3 centers are excellent, including colonic dissection, though not recommended during training. The countertraction method, as a technical help incorporated in the curriculum, should allow an efficace and wide spreading of ESD in Europe, including colonic location.

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Disclosure: Nothing to disclose

P1217

DEVELOPMENT OF MACHINE LEARNING MODELS TO PREDICT RISK OF PATHOLOGY OR NEED FOR INTERVENTION AMONGST ADULT PATIENTS UNDERGOING COLONOSCOPY DURING THE PANDEMIC

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Introduction: The number of colonoscopies performed yearly is continuously increasing around Europe. Accordingly, endoscopy services are coming under substantial service-delivery pressure, and waiting times were becoming unacceptable, even before COVID-19. Now units are faced with a crisis, beyond delivery. The best way to minimise this burden would be to identify predictors of pathology during colonoscopy. This calls for better risk-stratification of patients such that high-risk patients can be prioritised for colonoscopy and less invasive alternatives like capsule or virtual colonoscopy could be used for lower-risk patients.

Aims & Methods: **Aim:** To construct foundational machine-learning models which predict the likelihood of pathology and need for intervention at colonoscopy.

Methods: Colonoscopy records were anonymised. Predictors available within the dataset included: *sex, age, procedure indications and urgency of referral*. Outcomes of interest included: 'all-pathology' and 'interventional-pathology', where intervention (including biopsy) was required. Odds Ratios/Chi-Square statistics were calculated for all predictors. We then developed and internally validated multivariate logistic regression (LR) models, decision tree classifiers and artificial neural nets.

Results: 23,663 colonoscopies, performed on 18,677 individual patients were analysed. Mean age: 60.89; 50.91% Female. The most common indications for colonoscopy included: Polyp Surveillance[n=6137] (26%) and Bowel Cancer Screening (BCSP)[n=4508] (19%). 74.92%(+/-0.56%-95%CI) of tests contained some pathology; 64.84%(+/-0.61%-95%CI) contained 'interventional-pathology'. Significant ($p < 0.01$) predictors of pathology are listed in [Table 1]:

Predictor	'All-Pathology' OR(95%CI)	'All-Pathology' Pearson-Chi2	'Interventional-Pathology' OR(95%CI)	'Interventional-Pathology' Pearson-Chi2
Age: >55	3.51 (3.30-3.74)	1661.67	1.09 (1.02-1.15)	7.49
Sex: Male	1.77 (1.67-1.88)	2004.02	0.71 (0.67-0.74)	214.07
Indication: Previous-Polyps	3.34 (3.07-3.64)	836.47	2.42 (2.26-2.59)	672.50
Indication: BCSP	3.94 (3.55-4.38)	738.61	1.33 (1.23-1.42)	63.05

[Table 1: A Sample of Some Predictor Statistics from the Algorithm]

Multiple factors were combined to identify the best-case scenario for finding pathology: 97.6%(+/-0.93%-95%CI) of males, Aged >55, undergoing urgent colonoscopy for polyp surveillance, while only 21.79%(+/-6.06%-95%CI) of females, <55yrs, undergoing urgent colonoscopy for anaemia had any 'interventional-pathology'. Given the nature of the dataset, LR performed best and was able to obtain an optimised AUC of 0.75 for predicting 'all-pathology' and 0.70 for 'interventional-pathology' suggesting that this very simple algorithm holds significant predictive weight.

Subgroup analysis to assess distribution and frequency of polyps demonstrated their presence in 48% (n:11347) of procedures. However, the vast majority 70% (n:7943) of these procedures only contained diminutive (<10mm) polyps. In 23% (n:2605) of these procedures, polyps were only found in the right colon vs 47.7% (n:5408) only in the left.

Conclusion: Machine-learning algorithms can use simple pre-procedure parameters to predict the likelihood of finding significant pathology during colonoscopy. We have identified subgroups with a high and low probability of finding pathology requiring colonoscopic intervention. This approach can help to facilitate prioritisation of colonoscopic resource utilisation during this pandemic and appropriate diversion to non-interventional investigations like a capsule or virtual colonoscopy.

At the same mapping of the polyp-distribution implies that almost a quarter of polyps would be missed during flexible sigmoidoscopy based screening programmes, thus a strong argument to continue full colonoscopic bowel cancer screening during the pandemic can be made.

Disclosure: Nothing to disclose

P1218

IS TELEPHONE RE-EDUCATION PREVIOUS TO BOWEL PREPARATION A REAL ASSET?

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Introduction: Despite all the innovations in bowel preparation methods, the quality of bowel preparation in some patients undergoing colonoscopy remains a major limitation. Recently, some studies suggest that telephone re-education (TRE) before colonoscopy is associated with better quality of preparation.

Aims & Methods: To compare the quality of bowel preparation based on written, oral and telephone information (TRE) versus only written and oral information.

Single-center, prospective, randomized, blinded study. Exclusion Criteria were: age < 18 years, pregnant or breastfeeding women, patients with gastric obstruction, psychiatric disorders, chronic kidney disease with clearance of creatinine < 30 ml, heart failure class III-IV NYHA, laxative drugs use, chronic constipation (< 3 bowel movements/week), uncontrolled hypertension, bowel surgery or colostomy, severe ascites, bowel obstruction and refusal to participate in the study.

All patients received regular instructions during appointment (oral) and written by mail. Those scheduled for colonoscopy were randomly assigned to receive TRE two days before colonoscopy for bowel preparation or no TRE (control group). TRE was performed by an experienced nurse and it consisted of a phone call of about 10 min in which an explanation of the preparation with practical tips was given, and all the patients' doubts were clarified.

Results: After applying exclusion criteria, 613 patients were included, median age 61 (18-86) years, 53.5% male, 47.8% (n=293) received *Plenvu* and 52.2% (n=320) *Moviprep*. We verified that 205 (33.7%) of our population were on TRE group, 50.7% received *Plenvu* and 49.3% *Moviprep*.

Patients that received TRE were significantly older (63.0vs60.0;p=0.031). We found no other differences between the groups regarding gender, type of preparation, chronic co-morbidities and medication. Patients on the TRE more frequently performed colonoscopy in the morning period (78.5%vs55.2%; p< 0.001).

We found no differences in patients with or without TRE regarding adequate bowel preparation (Boston Bowel Preparation Scale ≥ 6 , with no subscore less than 2) (82.4%vs81.4%;p=0.762). When we compared the presence of adequate bowel preparation in both groups in the morning (78.3%vs71.7%;p=0.149) and in afternoon (95.5%vs93.4%;p=0.608), no statistical significant differences were observed.

Conclusion: In our study, we found no influence of telephone re-education (TRE) in the quality of bowel preparation. Therefore, good clarification during appointments and well-written information such as in our center to reinforce the importance of bowel preparation for the success of the colonoscopy seem sufficient for a good preparation.

Disclosure: Rosa B. has consulting services agreement with Medtronic®.

P1219

ONE-PERSON OPERATED ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASMS USING ENDOSABER

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Introduction: Endoscopic submucosal dissection (ESD) is a less-invasive local treatment for colorectal neoplasms. We invented a method of one-person operated ESD (OPO-ESD) that uses a novel needle-type knife, the Endosaber. Endosaber can cut, coagulate, and inject by itself. OPO-ESD eliminates the need for assistance and additional devices, such as injection needles and hemostatic forceps.

Aims & Methods: We conducted a prospective cohort study to investigate the feasibility and safety of OPO-ESD for colorectal neoplasms. Patients with 20-40mm colorectal neoplasms were enrolled and treated via OPO-ESD. One single operator, without an assistant, performed ESD for treating colorectal neoplasms using only the Endosaber. The outcomes of this study were the success rate of OPO-ESD, procedure time, the rates of en bloc, complete and curative resection, and complication rates.

Results: In total, 15 patients with 15 lesions were enrolled. The median size of resected lesions was 28 (interquartile range: 25-29) mm. OPO-ESD success rate was 100%. The median procedure time was 44 (29.5-53.5) min. En bloc, complete and curative resection rates were 100%, 93.3% and 86.7%, respectively. Complication rate was 6.7% (perforation: 0%, delayed bleeding: 6.7%).

Conclusion: OPO-ESD for colorectal neoplasms was successfully performed with favorable treatment outcomes and low complication rates. OPO-ESD reduces the amount of devices and assistance required, which might be a simple and cost-effective procedure for removing colorectal neoplasms.

Disclosure: Nothing to disclose

P1220

PIECEMEAL COLD SNARE POLYPECTOMY OF LARGE SESSILE SERRATED LESIONS IS SAFER AND EQUALLY EFFICACIOUS IN COMPARISON TO CONVENTIONAL ENDOSCOPIC MUCOSAL RESECTION

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Introduction: Large (≥ 20 mm) sessile serrated lesions (L-SSL) are premalignant and require endoscopic removal. Endoscopic mucosal resection (EMR) is the existing standard of care but carries a significant risk of serious adverse events including clinically significant post-EMR bleeding (CSPEB) and deep mural injury (DMI).

Aims & Methods: We examined the utility of piecemeal cold snare polypectomy (p-CSP) in L-SSL management by comparing technical success, adverse events and recurrence to conventional EMR outcomes. Data was collected prospectively in a multicentre setting (NCT01368289). All L-SSL referred for endoscopic resection were eligible. Lesions were resected in piecemeal using a dedicated thin-wire cold snare. A previous prospective cohort of L-SSL treated by conventional EMR was the comparator. The primary outcome was technical success and secondary outcomes were adverse events and recurrence. All L-SSL attempted for resection at index endoscopy were included for analysis. Per-lesion and per-patient analysis were applied where appropriate with per-patient analysis based on the largest lesion. Standard surveillance colonoscopies (SC) with routine scar assessment were conducted at 6 months (SC1) and 18 months (SC2) following the index procedure. L-SSL identified during follow-up were not eligible as to allow for per-patient analysis.

Results: Over 44 months to January 2020, 156 L-SSL in 121 patients were treated by p-CSP. The comparator cohort comprised of 406 L-SSL in 353 patients. Lesion size ranged up to 70mm with a median size of 25mm (IQR 20 - 30mm) and the majority were detected in the proximal colon. All 156 L-SSL (100.0%) were successfully resected. No adverse events occurred during or following p-CSP whereas CSPEB and DMI (including delayed perforation) were encountered in 5.1% and 3.4% of L-SSL treated by EMR,

respectively. Surveillance was completed in over 95% (SC1) and over 85% (SC2) of eligible patients. Recurrence rates following p-CSP were equally low in comparison to EMR at 4.3% vs 4.6% and 2.0% vs. 1.2% for SC1 and SC2, respectively.

Conclusion: In a large prospective cohort compared to EMR, p-CSP is equally efficacious with negligible recurrence in long-term follow-up and has eliminated the risk of perforation and delayed bleeding. P-CSP should be considered as the new standard of care for the treatment of L-SSL.

Disclosure: Nothing to disclose

P1221

PRECUTTING ENDOSCOPIC MUCOSAL RESECTION VERSUS ENDOSCOPIC SUBMUCOSAL DISSECTION OF LARGE (2-3 CM) FLAT COLORECTAL LESIONS

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Introduction: Complete & safe removal of large (≥2 cm) colorectal lesion is an area of concern. Endoscopic submucosal dissection (ESD) can effectively remove the large colorectal lesion compared to endoscopic mucosal resection (EMR). But ESD needs to more advanced skill, longer procedure time and high cost. Precutting endoscopic mucosal resection (EMR-P) is a modified EMR method to overcome the limitation of EMR. The aim of this study was to compare the efficacy and safety of EMR-P with ESD on the removal of the large flat colorectal lesion.

Aims & Methods: This was a retrospective analysis that performed for resection of large (2-3 cm) flat colorectal lesions in Seoul St. Mary's Hospital from January 2014 to December 2019. In this study, we excluded highly suspicious submucosal invasion (SMI) lesions, severe submucosal fibrosis (SMF) lesions resulting from resection attempts or chronic inflammatory disease, less-experienced operators, anorectal junction lesions. The primary outcome was R0 resection rate. The secondary outcome was *en bloc* resection rate and other variables.

Results: One hundred thirteen lesions in EMR-P group and 186 lesions in ESD group were included in the study. The mean (SD) size of the lesions was no significant difference in the EMR-P group compared to ESD group (22.88 ± 3.10 mm vs. 23.49 ± 3.57 mm, *P*=0.137). R0 resection rate was no significant difference in EMR-P group compared to ESD group (90.3% vs. 93.5%, *P*=0.302) and *en bloc* resection rate was 93.8% in EMR-P group and 97.8% in ESD group (*P*=0.110), respectively. Mean (SD) procedure time was significantly shorter in the EMR-P group compared to ESD group (10.6 ± 6.5 min vs. 38.6 ± 20.9 min, *P*< 0.001). Hospitalization was significantly lower in the EMR-P group compared to ESD group (13.3% vs. 98.0%, *P*< 0.001). R1 resection was only 2 cases in EMR-P group. The complication rate was no significant difference between both groups. Mean (SD) follow-up duration was significant difference in both groups (18.3 ± 10.3 vs. 13.7 ± 7.1, *P*< 0.007). No recurrences occurred in both groups.

Conclusion: EMR-P is not inferior to ESD for R0 resection of large (2-3 cm) flat colorectal lesions and significantly shorter procedure time and lower rate of hospitalization are required than ESD.

Disclosure: Nothing to disclose

P1222

CONECCT CLASSIFICATION: THE BEST DAILY WAY TO ELIMINATE SUBMUCOSAL CARCINOMA IN LARGE SUPERFICIAL LESIONS

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Introduction: Several classifications have been proposed to predict histology of superficial colorectal lesion, based on overt and covered endoscopic signs of carcinoma.

We created the CONECCT classification (Colorectal Neoplasia Classification to Choose the Treatment) which is an all-in-one table, mixing Paris, SANO, KUDO, WASP, LST, NICE, JNET classification in order to simplify characterization without using magnification. It differentiates low-risk lesions (CONECCT IIA), needing endoscopic resection that could be piecemeal EMR according to the size, from high risk of submucosal cancer lesion (CONECCT IIC) requiring absolute en-bloc resection.

We performed a real-world validation study for the prediction of submucosal carcinoma in lesions larger than 20 mm referred to an expert center for endoscopic submucosal dissection.

Aims & Methods: We performed a prospective bi-centric study in two European expert-centers. Lesions referred for colorectal ESD were included by four trained operators.

Optical diagnosis data were recorded before resection, just before the ESD procedure, according to Paris, LST, Sano, Kudo and CONECCT classifications with last generation endoscopes FUJIFILM 760 or OLYMPUS 190 under white light and virtual chromoendoscopy, without using magnification.

Sensitivity (Se), Specificity (Spe), Positive predictive value (PPV) and Negative predictive value (NPV) of LST NG, macronodule larger than 1 cm, SANO IIIA, Paris O-IIC ulceration and CONECCT IIC were calculated and compared for predicting at least submucosal carcinoma according to histology.

Results: Between May 2013 and December 2019, 993 colorectal lesions were removed by ESD.

Macroscopic features: Overall 663 lesions were assessed (mean size 57.9mm) with complete characterization data (LST, presence of macronodule larger than 1cm, Paris, SANO, KUDO and CONECCT). 66.4% were LST-G, 19% LST-NG and 12.8% protruding lesions. 76% were classified CONECCT IIC, 40% SANO IIIA, 13.9% had a Paris O-IIC ulceration and 53.4% had a macronodule.

Histological analysis: LGD (Vienne 3) : 32.6%; HGD (Vienne 4.1 and 4.2) : 37%; IM carcinoma (Vienne 4.4): 20.7%; Sm < 1000µm (T1a): 4.4%, Sm > 1000µm (T1b) : 3.9% ; T2 : 0.6%.

Diagnostic accuracy: Diagnostic accuracy of CONECCT classification was Se 100%, Spe 26.16%, PPV 11.51%, NPV 100% (95% CI 0.59-0.64). CONECCT IIC classification was significantly more sensitive than other risk factors independently: Se SANO IIIA 66.1%, Se macronodule 76.27%; Se Ulceration 27.12% (*p*<0.0001).

In multivariate analysis, surface ulceration, SANO IIIA area and rectosigmoid location were significantly associated with submucosal carcinoma (*p*=0.003, *p*=0.012 and *p*=0.014 respectively).

When the number of poor prognostic criteria (NG LST, macronodule >1 cm, Ulceration, SANO IIIA) is higher, percentage of at least submucosal carcinoma is increased (0 criterion: 0%, 1 criterion: 8.5%, 2 criteria: 11.9%, 3 criteria: 23.6% (*p*< 0.0001).

No difference was observed using FUJIFILM or OLYMPUS with either BLI or NBI system (AUC SANO IIIA FUJIFILM: 0.63 vs AUC SANO IIIA OLYMPUS: 0.62, $p = 0.784$).

Conclusion: CONECCT classification is the best available classification to determine the risk of submucosal carcinoma and to choose the endoscopic treatment for large superficial lesions with a 100% Se and NPV. This table is efficient with non-magnification scope of different suppliers. A stratified approach oriented by the number of poor prognostic criteria allows an accurate determination of the submucosal carcinoma risk, a key step to determine what lesions need an en-bloc resection by ESD.

Disclosure: Nothing to disclose

P1223

ARTIFICIAL INTELLIGENCE FOR COLORECTAL POLYP DETECTION: A VALIDATION TRIAL WITH REAL-TIME UNBLINDING

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Introduction: Artificial intelligence (AI) has recently entered the world of endoscopy, especially for polyp detection and characterization. Many novelties have been introduced and tested with promising results to marginalize endoscopists' miss rates and increase polyp detection.

Aims & Methods: We aim to prospectively validate a novel and deep learning computer aided detection tool (CADE) for polyp detection with an entirely new development background. We wanted to test the performance of this system compared to experienced endoscopists as gold standard in a multicenter prospective clinical trial with blinding of the endoscopists by introducing a second observer for the AI output in the room.

Between August 2018 and November 2019 a deep learning framework for polyp detection was developed and trained based upon 131,619.00 frames of 825 polyps from 205 different patients and implemented in a bedside module. This system was optimized with the ability of incorporating time-related information in memory cells, making this system completely different from classical convolutional neural networks and allowing a better recognition. From November 2019 till February 2020 we used this artificial intelligence (AI) tool during daily colonoscopies performed by experienced endoscopists (adenoma detection rate (ADR) > 35%) in patients of at least 18 years old. We introduced a completely new concept with the endoscopist unblinded for the CADE systems's presence but blinded from the AI tool's output by an independent second observer watching the AI-screen during real-time withdrawal and categorizing the outcome in four possible outcomes: (1) an obvious false detection (stools, air bubbles, ...), (2) a 'other positive' detection being a detection only made by the CADE system where to the endoscopist is asked to return, if this is a polyp that is an extra detection if not it is a false positive, (3) a false negative detection being a polyp missed by the AI-system and (4) a true positive detection being a polyp found by both the endoscopist and the CADE system. We enrolled 357 patients from 3 European hospitals. After exclusion 294 patients were included for study analysis.

Results: In 294 patients a total of 606 polyps was found. The number of true positive detections was 574 (94.7%), the number of extra detections was 11 (1.8%) and the number of missed lesions was 21 (3.5%) resulting in a CADE's accuracy of 0.965 (95% CI: 0.951 ; 0.980). The accuracy of the high

detecting endoscopists was 0.982 (95% CI: 0.971 ; 0.992). When comparing difference in these two proportions, the AI tool was non-inferior to the endoscopist in terms of accuracy with a difference of -0.017 (95% CI: -0.0378 ; 0.0047%; $p < 0.001$) and a non-inferiority margin of 5%. The system's miss rate was 3.47% and the miss rate of the endoscopist was 1.82%. The false positive rate of the CADE system was 1.4 per minute for an average clean withdrawal time of 10.3 minutes.

Conclusion: In this pilot trial we used a novel and unique study design that allows validation of CADE for polyp detection without patient randomization and with blinding of the endoscopists. We showed that our AI-system for polyp detection performs with a high accuracy of 96.5% and is non-inferior to high detecting endoscopists (ADR > 35%). In addition, inclusion of recurrent neural networks, resulted in a low false positive rate of 1.4 per minute, indicating that our system will not frequently interfere unnecessary with the endoscopists.

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P1224

ASSOCIATION OF ASPECTS OF PROCEDURE WITH REPORTING OF PEDUNCULATED AND NON-PEDUNCULATED LESIONS: OBSERVATIONS FROM THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION QUESTIONNAIRE

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Introduction: The development of the European Colonoscopy Quality Investigation (ECQI) Group questionnaire has been previously described (UEGW 2015 and 2016).^{1,2}

Aims & Methods: To assess how aspects of a procedure associate with reporting of pedunculated (Paris classification Ip and Isp) and non-pedunculated (all other Paris classifications) lesions. We analysed data collected between 2/6/16 and 30/4/18.

Results: Of 6445 procedures, 2621 reported a polyp in at least one segment (40.7%). Pedunculated lesions were reported in 601 procedures and non-pedunculated lesions in 2255 procedures.

Use of chromoendoscopy was significantly associated with the reporting of pedunculated lesions (15.3% vs 8.0%, $p < 0.0001$ overall, $p \leq 0.01$ in each segment) and non-pedunculated lesions (68.2% vs 27.4%, $p < 0.0001$ overall, $p < 0.0001$ in each segment).

Reporting of non-pedunculated lesions was significantly increased in association with use of sedation (37.2% vs 29.3%, $p<0.0001$ overall, $p\leq 0.001$ in each segment), high-definition (HD) equipment (38.7% vs 22.5%, $p<0.0001$ overall, $p<0.0001$ in each segment), and assistive technology (42.9% vs 34.2%, $p<0.0001$ overall, $p\leq 0.022$ in each segment).

Higher rates were seen with the use of Endocuff (57.7%) and cap-assisted (53.7%) versus when other assistive technologies were used (40.8%). Reporting of pedunculated lesions was not associated with any of these factors (sedation $p=0.069$, HD equipment $p=0.156$, assistive technology $p=0.317$).

The time of day that the procedure was performed (morning, afternoon or evening) was not associated with the reporting of either pedunculated or non-pedunculated lesions.

	Right	Transverse	Left	Any segment
Any polyp	1328	723	1645	2621
Pedunculated	144	89	447	601
Non-pedunculated	1203	633	1261	2255

[Procedures in which a polyp was reported by type and colon segment]

Conclusion: The reporting of both pedunculated and non-pedunculated lesions was increased when chromoendoscopy was used. Use of sedation, HD equipment and assistive technology improved detection of non-pedunculated lesions but had no association with pedunculated lesion reporting.

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Disclosure: Ono A, Amaro A, Agrawal A, Hüniger M, Petruzzello L, Toth E - Consultant & advisory board participant to Norgine; Spada C - Consultant fee from Norgine; Brink L - Consultancy & Advisory Board participant to Norgine; AMBU: Fischbach W - Consultancy and Advisory Board participant to Norgine; Speaking - Abbott, Bio Merieux, Falk; Advisory speaking - Aptalis, Fresenius Biotech, Pfizer; Advisory - Boehringer Ingelheim, med update: Kinnunen U - Norgine and Olympus (European NBI Expert Training Group); Riemann JF - In terms of ECQI, consultant to Norgine, otherwise no conflict of interest; Amlani B - Employee of Norgine; Fuccio L - No conflict of interest; Koulaouzidis A - No relevant conflict of interest.

P1225

A MULTI-CENTRE ENDOSCOPIST BLINDED RANDOMIZED CONTROLLED TRIAL TO COMPARE TWO BOWEL CLEANSING PROTOCOLS AFTER A COLONOSCOPY WITH INADEQUATE BOWEL PREPARATION

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Introduction: Failed bowel preparation is common during colonoscopy, yet the optimal purgative regimen to use for the next attempt is unknown. The objective of this study was to compare the efficacy, tolerability, and safety of two regimens at supratherapeutic doses for use in this population of difficult to cleanse colons.

Aims & Methods: A multi-centre phase III endoscopist blinded randomized controlled trial (NCT02976805) was conducted in patients who failed bowel preparation, defined according to the U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF) as the inability to exclude polyps >5 mm in size and requiring a shortened colonoscopy interval. Patients who had an inpatient colonoscopy, were non-adherent or had taken off-label bowel preparation, were at risk for fluid or electrolyte disturbances, or had a contraindication to bowel preparation were excluded. Regimen A consisted of 15 mg of bisacodyl and 2+2 L of split dose polyethylene glycol electrolyte solution (PEG) and Regimen B consisted of 15 mg of bisacodyl and 4+2 L of split dose PEG. Both were preceded by a low fiber diet on days 3 and 2 before colonoscopy followed by a clear fluid diet the night before and morning of the procedure. Dietary and purgative intake records were completed by patients to assess adherence. The primary outcome was adequate bowel preparation, defined as a Boston Bowel Preparation Scale (BBPS) total score ≥ 6 with all segment scores ≥ 2 . Secondary outcomes were adequate bowel preparation using the USMSTF definition, median BBPS, and adenoma detection (ADR), advanced adenoma detection (aADR), sessile serrated polyp detection (SSPDR), polyp detection (PDR), and cecal intubation (CIR). Adverse events were assessed at the time of the colonoscopy and with a telephone call 14 days later. All analyses were pre-specified and followed an intention-to-treat principle.

Results: Between February 1, 2017 to December 15, 2019, 250 subjects were screened at four large academic centres in Canada, of which 195 were randomized: 96 to Regimen A and 99 to Regimen B. The mean (SD) age was 60.6 (11.4) years, 87 (45.1%) were female, 50.3% had a history of constipation or were on a medication known to cause constipation, and the median (IQR) BBPS total score was 3 (1,4) at index colonoscopy. Overall, Regimen B was not superior to Regimen A in achieving adequate bowel preparation using the BBPS definition (87.6% vs. 91.1%, $p=0.45$) or the USMSTF definition (85.4% vs 91.1%, $p=0.24$), nor was it superior with respect to the median BBPS score (7 vs 7, $p=0.50$), mean ADR (31.5% vs 37.8%, $p=0.37$), aADR (11.2% vs 18.9%, $p=0.15$), SSPDR (5.6% vs 8.9%, $p=0.40$), PDR (55.1% vs. 58.9%, $p=0.60$) or CIR (92.1% vs 96.7%, $p=0.19$), respectively. There was no significant difference in median tolerability on a visual analogue scale (7 vs. 8, $p=0.58$) although Regimen A had a higher adherence rate (88.2% vs. 74.7%, $p=0.02$) and greater willingness to undergo the bowel preparation again (91.2% vs. 66.2%, $p<0.001$). The only bowel preparation related serious adverse event occurred in a patient randomized to Regimen B who was admitted to hospital for vomiting after colonoscopy.

Conclusion: Regimen A is highly efficacious, well tolerated, and can be used for patients who have previously failed first line bowel preparations. The additional 2L of PEG in Regimen B did not improve bowel preparation.

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P1226

CORRELATION BETWEEN REAL-TIME ENDOSCOPIC POLYP EVALUATION AND SUBSEQUENT HISTOLOGICAL OUTCOME - IS IT TIME TO ADOPT A 'RESECT AND DISCARD' POLICY FOR DIMINUTIVE POLYPS?

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Introduction: The current standard during colonoscopy procedures is to identify and resect polyps and send the samples for histological evaluation. However, a 'resect and discard' approach is proposed by several authors for small non-adenomatous polyps. This serves to reduce the procedural time, screening costs and risk of complications associated with colonoscopy.

Aims & Methods: The aim of this study is to explore if transition to the above approach would be safe in clinical practice. In order to assess the ability of the endoscopists to safely distinguish adenomas and non-adenomatous polyps we conducted a retrospective study of all the colonoscopies undertaken between 1st January 2019 to 31st December 2019 in a UK tertiary hospital. Data about the endoscopists' training, as well as the procedure and polyp characteristics were collected. The procedure report was used to review if the endoscopist identified and characterised each polyp; the standard characterisation method was the Kudo classification. Polyp sizes were further categorised to 1-5mm, 6-10mm, and >10mm. The true nature of polyps was determined using the histology reports and compared to the endoscopic diagnosis. We excluded polyps if there was ambiguity about their sampling location or their histology result was inconclusive.

Results: A total of 3061 colonoscopies were performed during the study period. We analysed the 949 endoscopies where polyps were detected. The majority of procedures were performed by consultants (82.7%), followed by trainee endoscopists (13.1%) and endoscopy nurses (4.2%). 719 (75.8%) colonoscopies took place within normal working hours. 2487 polyps were detected of which 1305 had documented Kudo classification. A total of 1029 polyps were included in the study and reviewed against their histology. Most polyps were identified as Kudo type IIIS (39.4%), followed by IIIL (37.4%), II (13.7%), IV (6.4%) and V (0.78%). Polyps were correctly classified as adenomas in 84.1% of cases in comparison to 66.4% polyps correctly classified as hyperplastic. There was no significant difference in correct classification of adenomas between different speciality groups (gastroenterologists, general surgeons and specialist nurses, $p=0.59$), endoscopists' grade ($p=0.93$), buscopan use ($p=0.83$), bowel prep ($p=0.54$), comfort score during the procedure ($p=0.61$), or timing of the procedure ($p=0.053$). The endoscopic diagnosis of adenoma for Kudo IIIS and polyp size 1-5 mm had significantly lower correct classification compared to the other groups ($p<0.001$ and $p=0.01$ respectively). The size of hyperplastic polyps did not affect the likelihood of correct classification ($p=0.89$). There were 7 histologically proven polypoid cancers, all of which were correctly identified as Kudo V.

Conclusion: In this retrospective observational study, optimal correlation was observed between identification of cancerous polyps during endoscopy and subsequent histology. On the other hand, differentiation of adenomatous versus hyperplastic polyps was less satisfactory, especially for diminutive polyps (1-5 mm). Therefore, "resect and discard" policy cannot adequately guide us in polyp surveillance scheduling.

Disclosure: Nothing to disclose

P1227

ANNUAL COLONOSCOPY VOLUME IS NOT PREDICTIVE OF COLONOSCOPY QUALITY - FINDINGS FROM THE SOUTHWEST ONTARIO COLONOSCOPY COHORT

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Introduction: Some endoscopy units and colorectal cancer screening programs mandate a minimum number of colonoscopies be performed each year for physicians to maintain certification. However, prior studies examining the relationship between annual colonoscopy volume and measures of colonoscopy quality, such as adenoma detection rate (ADR), had inadequate sample sizes, lacked confounding control, or were conducted at single centres thereby limiting generalizability. The objective of this study was to determine if annual colonoscopy volume was predictive of colonoscopy quality metrics.

Aims & Methods: The Southwest Ontario Colonoscopy cohort consists of all patients who underwent colonoscopy between April 2017 and October 2018 at 21 academic and community hospitals serving a large geographic area in Southwest Ontario. Data was collected through a mandatory quality assurance form that was completed by the endoscopist after each procedure. Pathology reports were manually reviewed. Physician annualized colonoscopy volumes were compared by correlation analysis to each quality-related outcome, by means of the area under the receiver operating characteristics curve (AUROC), and logistic regression. The prognostic value of colonoscopy volume was also adjusted for case-mix and potential confounders in separate regression analyses for each outcome. The primary outcome was ADR. Secondary outcomes were polyp detection rate (PDR), sessile serrated polyp detection rate (SSPDR), and cecal intubation.

Results: A total of 47,195 colonoscopies were performed by 75 physicians (37.5% by gastroenterologists, 60% by general surgeons, 2.5% others). Overall ADR (range) and PDR (range) were 26.2% (7-51%) and 40.5% (14-93%), respectively. There were no clear relationships between annual colonoscopy volumes and study outcomes. On crude analysis, colonoscopy volume was not associated with ADR (OR 1.03, 95% CI 0.96-1.10, $p=0.48$) and corresponded to an AUROC not significantly different from the null (AUROC 0.52, 95% CI 0.43-0.61, $p=0.65$). Multi-variable regression adjusting for case-mix also demonstrated no predictive value of annual colonoscopy volume for the primary outcome (OR 1.03, 95% CI 0.94-1.12, $p=0.55$). Similarly, analyses of secondary outcomes failed to find an association between colonoscopy volume and PDR, SSPDR, or cecal intubation (Table 1).

Conclusion: Annual colonoscopy volumes do not predict ADR, PDR, SSPDR, or cecal intubation.

Outcome	Uni-variable OR (95% CI)	p-value	AUROC (95% CI)	p-value	Multi-variable OR (95% CI)	p-value
ADR	1.03 (0.96-1.10)	0.48	0.52 (0.43-0.61)	0.65	1.03 (0.94-1.12)	0.55
PDR	1.04 (0.97-1.11)	0.27	0.55 (0.49-0.65)	0.33	1.00 (0.91-1.1)	0.99
SSPDR	1.09 (0.96-1.24)	0.18	0.55 (0.45-0.66)	0.32	1.08 (0.96-1.2)	0.20
Cecal intubation	0.94 (0.89-0.99)	0.03	0.57 (0.49-0.65)	0.73	0.96 (0.89-1.03)	0.28

[Table 1. Results of unconditional & conditional approaches for examining predictive value of annual colonoscopy volume for quality related outcomes]

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P1228

DOUBLE-CLIP TRACTION IS SUPERIOR TO THE POCKET CREATION METHOD FOR COLONIC ESD: A RANDOMIZED STUDY IN AN EX VIVO MODEL

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Introduction: In Western countries, debates between ESD vs piece-meal EMR as the best treatment for large colorectal adenomas persist regarding the difficulty of ESD the colon, and the safety and relatively good results of piece-meal endoscopic mucosal resection (EMR). Pocket creation method (PCM) and double clip countertraction (DCT) are two strategies recently published to facilitate ESD in this challenging situation. The aim of this randomized animal study was to compare the procedural outcomes between these two procedures.

Aims & Methods: Randomized animal study to compare PCM and DCT strategies for colonic ESD on ex-vivo models (bovine colon). Hybridknife type T was used to inject normal saline tinted with a small amount of blue dye in all procedures. Randomization was stratified according to the use of gravity assist.

Primary endpoint was the difference in resection speed between PCM and DCT strategies.

The secondary endpoints were the differences between the two strategies in terms of technical success rate, perforation rate and dissection score, as well as the results based on the presence versus absence of gravity assist. Three young operators performed all procedures. However, all had benefited from theoretical training and technical feedback by two French experts.

Results: Resection speed, was significantly higher in the DCT group than in the PCM group (56.3 vs. 31.6 mm²/min, p=0.01).

Technical success rate, defined as en bloc resection in under 60 min, was significantly better in the DCT group than in the PCM group (100% vs. 84.4%, p= 0.024), perforation rate was lower (3.3% vs. 18.8%, p=0.012), difficulty score was better (2.4 vs. 6.2, p<0.0001) as was procedure duration (24.2 vs. 40.2 min, p<0.0001).

DCT performed better with gravity assist than without it in terms of the resection speed (73.1 vs. 39.5 mm²/min, p=0.049), but technical success rate (100% vs. 100%, p=1), perforation rate (0% vs. 0%, p=1) and difficulty score (2 vs. 2.9, p=0.14) (Figure 5) were similar regardless of the presence of gravity assist. In the PCM group, the presence of gravity assist showed better results compared with its absence in terms of resection speed (38.8 vs. 21.1 mm²/min, p=0.005), technical success rate (100% vs. 66.6%, p=0.015) and difficulty score (4.6 vs. 7.9, p=0.0001).

Finally, DCT in the absence of gravity assist was superior to PCM in the presence of gravity assist in terms of the difficulty score (2.9 vs. 4.6, p=0.016), but the resection speed (39.5 vs. 38.8 mm²/min, p=0.93) and technical success rate (100% vs. 100%, p=1) were similar between the two strategies.

Conclusion: DCT was superior to PCM for ESD in our validated bovine colon model. This strategy is inexpensive, easy to use and adaptive. It might facilitate the widespread use of colonic ESD in Western countries and change Western ideas regarding the use of colonic ESD compared with piece-meal EMR for large benign lesions.

Disclosure: Nothing to disclose

P1229 WITHDRAWN

P1230

IMPROVED ADENOMA DETECTION RATE WITH HIGH DEFINITION COLONOSCOPY

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Introduction: Colonoscopy has become a cornerstone in early diagnosis and prevention of colorectal cancer (CRC). Adenoma detection rate (ADR) is an important key performance indicator that has been shown to be directly related to interval CRC (1). Advances in endoscopy have paved the way for improved polyp detection and resection. High definition (HD) image quality may increase ADR.

Aims & Methods: Our aim was to compare polyp detection rates between patients whose procedure was carried out with a HD vs a standard definition (SD) colonoscope. This was a retrospective study analysing an electronic endoscopy database from an academic teaching hospital in Dublin, Ireland. All colonoscopies carried out from January 1st to December 31st 2018 were screened. Average-risk screening colonoscopies were analysed. The unit's overall polyp detection rates, ADR, clinically significant serrated detection rate (CSSDR) and proximal serrated detection rate (PSDR) were calculated.

Results: 5,177 colonoscopies were screened, 967 of which were included in the analysis. The mean patient age was 67.7 years. Bowel prep was described as excellent in 18.9% of cases and adequate in 60.5%. The colonoscopies included in the study were performed for polyp surveillance (62%), previous history of CRC (24%), family history of CRC (10%) or screening (3%). The overall ADR was 37%, PSDR 17% and CSSDR 12%. When comparing the HD to SD colonoscopies there was an increase in all polyp detection rates in the HD colonoscope group. There was a statistically significant difference between the ADR in the HD group (41%) vs the SD group (28%) (P<0.05). A higher PSDR and CSSDR was achieved in the

HD group however this did not reach statistical significance (table 1.). Patient demographics were compared between HD/SD groups to evaluate for any confounding factors. There was a statistically significant difference in the quality of the bowel prep, a larger portion in the SD group were categorized as excellent prep (24.4% vs 17.1) compared with the HD group.

Conclusion: ADR was significantly higher in the HD colonoscopy group. Increases in polyp detection rate (PDR), PSDR and CSSDR were also seen although not reaching statistical significance. It stands to reason that a high definition picture quality will allow more colonic polyps to be detected, in particular smaller, more subtle lesions. It is however reassuring to see evidence to support this hypothesis.

To date the published data has shown minimal improvements in ADRs with improved image quality. A large meta-analysis reviewing 5 studies with 4,422 patients found marginal differences between HD and standard definition colonoscopy (2).

Similarly a prospective cohort study on 130 patients found that the HD colonoscopes did not lead to a statistically significant improvement in ADR or hyperplastic polyp detection (3).

Another study evaluating white light endoscopy (WLE) vs narrow band imaging (NBI) with patients being scoped using a HD colonoscopy found a very high overall ADR (66%). Although there was no difference between the NBI and WLE, the high ADR was felt to be attributable to the HD image. No standard definition colonoscopes were used for comparison however, so the study was not designed to answer this question (4).

To our knowledge this is one of the first studies to show a significant improvement in ADR when using HD colonoscopes.

	HD Scope (n=725)	SD Scope (n=244)	P-Value
ADR (%)	41	28	<0.05
PSDR (%)	18	15	0.132
CSSDR (%)	13	9	0.118

[Table 1. Polyp detection rates HD vs SD]

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Disclosure: Nothing to disclose

P1231

1L NER1006 REPRODUCIBLY EXCEEDS THE EUROPEAN SOCIETY OF GASTROINTESTINAL ENDOSCOPY MINIMUM TARGET RATE OF 90% ADEQUATE-LEVEL CLEANSING SUCCESS IN ALL COLON SEGMENTS WHEN ASSESSED BY TREATMENT-BLINDED CENTRAL READERS USING TWO VALIDATED COLON CLEANSING SCALES

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Introduction: NER1006 is the first 1L polyethylene glycol (PEG)-based bowel preparation. In two randomized controlled phase 3 clinical trials, NER1006 showed non-inferior overall adequate colon cleansing success and high-quality right colon cleansing success versus 2L PEG+ ascorbate (2LPEG; MORA trial) and oral sulfate solution (OSS; NOCT trial) [1,2]. Adequate cleansing success is particularly difficult to achieve in the right colon versus other colon segments [3]. We analysed the capacity of NER1006 to attain adequate-level cleansing success in the right colon versus all other colon segments in the MORA and NOCT trials.

Aims & Methods: This post-hoc analysis of the MORA and NOCT trials assessed the adequate cleansing success attained by NER1006 in the right colon versus other colon segments. Patients included in both trials were males and females aged 18-85 years and received NER1006 either as a two-day evening/morning split-dosing regimen (N2D) or a same-day morning-only dosing regimen (N1D). This analysis only included patients who underwent colonoscopy with segmental scores assigned by treatment-blinded central readers using the Harefield Cleansing Scale (HCS; primary endpoint) and the Boston Bowel Preparation Scale (BBPS; secondary endpoint). Adequate-level cleansing is defined as a segmental score of at least 2 on both HCS (range 0-4) and BBPS (range 0-3). The adequate cleansing success rates were calculated using scores based on video recordings and compared versus the right colon scores using the 2-sided t-test.

Results: 532 of 550 (97% MORA) and 255 of 276 (92% NOCT) randomized patients who received NER1006 were included in this analysis. In both trials, NER1006 achieved an adequate cleansing success rate in the right colon comparable to that in all other colon segments (Table 1).

Clinical trials	MORA		NOCT	
	N2D (N=262)		N1D (N=270)	
NER1006 regimens	HCS	BBPS	HCS	BBPS
Right 2+ (n/N)	98.1% (257/262)	96.9% (254/262)	95.2% (257/270)	93.7% (253/270)
Transverse 2+ (n/N)	99.6% (261/262)	99.2% (260/262)	96.3% (260/270)	96.3% (260/270)
2-sided p-values vs right colon	P=0.101	P=0.056	P=0.524	P=0.168
Left *2+ (n/N)	98.9% (259/262)	97.7% (256/262)	95.6% (258/270)	92.6% (250/270)
2-sided p-values vs right colon	P=0.477	P=0.589	P=0.838	P=0.610
Sigmoid 2+ (n/N)	98.1% (257/262)		94.1% (254/270)	
2-sided p-values vs right colon	P=1.000		P=0.568	
Rectum 2+ (n/N)	99.2% (260/262)		96.3% (260/270)	
2-sided p-values vs right colon	P=0.254		P=0.524	

[Table 1. Adequate cleansing success rates in the right colon versus other colon segments as assessed by central readers using the HCS and BBPS.]

*When scoring using the BBPS, the left colon includes the sigmoid and rectum segments.

When using the HCS, in the MORA study N2D achieved 98.1% versus 99.6%, 98.9%, 98.1% and 99.2% ($P \geq 0.101$ for all comparisons) of adequate-level cleansing success in the right colon versus transverse, left, sigmoid and rectum segments respectively. N1D achieved 95.2% versus 96.3%, 95.6%, 94.1% and 96.3% ($P \geq 0.524$ for all comparisons). In the NOCT study N2D also achieved adequate-level cleansing success in excess of 95%, namely 96.9% versus 96.9%, 96.5%, 96.9% and 96.5% ($P \geq 0.806$). When using the BBPS, the segmental adequate-level cleansing success rates were comparable in the right colon versus the transverse or left colon. In MORA, N2D achieved 96.9% versus 99.2% and 97.7% ($P \geq 0.056$), while N1D achieved 93.7% versus 96.3% and 92.6% ($P \geq 0.168$). In NOCT, N2D achieved 94.1% versus 94.5% and 92.5% ($P \geq 0.479$).

Conclusion: In patients who had colonoscopy, 1L NER1006 demonstrated high and comparable levels of adequate cleansing success in the right colon versus all other colon segments. These results exceeded the minimum performance target of 90% set by the European Society of Gastrointestinal Endoscopy, and were reproducible across two randomized controlled clinical trials and across two validated colon cleansing scales.

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P1232

HIGH PREVALENCE OF LIVER DISEASE AND OBESITY AMONGST A COLONOSCOPY POPULATION

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Introduction: Western populations demonstrate a growing burden of obesity, Non-Alcoholic Fatty Liver Disease (NAFLD).^{1,2} Our aim was to assess the burden of liver disease, obesity and metabolic syndrome amongst a population attending for colonoscopy.

Aims & Methods: The OSCAR study was a cross sectional study recruiting eligible patients from 12 sites attending for colonoscopy as part of a national Bowel Cancer Screening Programme or due to symptoms. Patients' completed a medical history and lifestyle questionnaire (including AUDIT-C [screening questionnaire for alcohol excess; ≥ 5 requires further assessment]), provide blood samples, and had height/weight/waist circumference measured. Age-adjusted FIB-4 score, Fatty Liver Index³ (FLI) were measured (>60 highly predictive of hepatic steatosis). Here we report the prevalence of liver disease, obesity and metabolic syndrome in a population attending colonoscopy.

Results: 1430 patients were recruited (screening 410 [29%]; symptomatic 1020 [71%]). The table below depicts the patient characteristics of our study recruits.

34 patients (2.37%) had a prior diagnosis of NAFLD. 553 patients (44.4%) had a raised FLI >60 , and 149 (26.9%) of these had indeterminate or abnormal FIB-4. 158 patients (12.2%) had ALT >40 U/L. Of these, 67 (46.5%) had an indeterminate or abnormal FIB-4. 7 patients had ALT $\geq 3 \times$ ULN, of whom only 1 had a prior diagnosis of liver related problem. Of 57 patients with abnormal FIB-4 score, 52 (91%) had not previously been diagnosed with liver disease. 1130 patients in our study (79%) consumed alcohol. Of these 593/1130 (52.5%) scored ≥ 5 in the AUDIT-C questionnaire and 169/1130 (15%) drank above recommended limits.

Conclusion: In a population attending colonoscopy, the burden of fatty liver disease, obesity and metabolic syndrome was high. Many individuals consumed alcohol to excess. These factors are associated with a range of adverse health outcomes, but are potentially modifiable. Endoscopy may provide a "teachable moment" for delivering brief health behaviour interventions.

Variable	N (%)
Sex	M 698 (48.8%)
Age	Median 59 $\pm$ 13.7 years
Obesity (WHO: BMI >30)	487 (34.2%)
Central obesity (Waist circumference: M >94 cm, F >80 cm)	1091 (77.2%)
Hypertension	480 (33.6%)
Type II Diabetes	182 (12.7%)
Raised HbA1c in non-diabetics	103 (7.2%)
Raised total cholesterol (>6 mmol/L)	255 (19.6%)
Raised triglycerides (>1.7 mmol/L)	262 (20.2%)
Metabolic syndrome (NCEP ATP III criteria)	256 (17.9%)

[Study patient characteristics]

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P1233

ARTIFICIAL INTELLIGENCE FOR POLYP DETECTION DURING COLONOSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Artificial intelligence (AI)-based polyp detection systems during colonoscopy aim to increase lesion detection and improve colonoscopy quality. We performed a systematic review and meta-analysis of randomized controlled trials to determine the value of AI-based polyp detection systems for detection of colorectal polyps and adenomas.

Aims & Methods: We performed systematic searches in MEDLINE, EMBASE and Cochrane CENTRAL for prospective diagnostic accuracy studies that directly compared colonoscopy with and without AI-based polyp detection systems in adults. Two independent reviewers screened studies and assessed eligibility, certainty of evidence, and risk of bias. We compared colonoscopy with and without AI by calculating the pooled relative and absolute risk and mean differences - with 95% confidence intervals - for detection of polyps, adenomas, and advanced adenomas.

Results: Out of 1,548 potentially relevant titles published until February 12, 2020, five randomized trials (Table 1) were eligible for analysis. Colonoscopy with AI-based polyp detection systems increased adenoma detection rates (ADR) and polyp detection rates (PDR) compared to colonoscopy without AI-assistance: ADR with AI 29.6% (95% confidence interval, 22.2-37.0), versus 19.3% (12.7-25.9) without AI (relative risk [RR] 1.52, [1.31-1.77], high certainty); PDR 45.4% (41.1-49.8) with AI, versus 30.6% (26.5-34.6) without AI (RR 1.48, [1.37-1.60], high certainty). There was no difference in detection of advanced adenomas between the two groups (mean number of advanced adenomas per colonoscopy 0.03 for each, high certainty). Mean number of adenomas per colonoscopy were higher for small adenomas (≤ 5 mm) with AI compared to non-AI colonoscopy (mean difference 0.15, [0.12-0.18]), but not for larger adenomas (> 5 - ≤ 10 mm: mean difference 0.03, [0.01-0.05]; > 10 mm: mean difference 0.01, [0.00-0.02], high certainty). Data on cancer are unavailable.

Conclusion: AI-based polyp detection systems during colonoscopy increase detection of small, non-advanced adenomas and polyps, but not advanced adenomas.

Study	Design	No. of Patients (AI; non-AI)	Men/Women (n)	Mean age (AI; non-AI)	Colonoscopy indication, n (%)	AI system
Wang 2019	RCT, non-blinded	1058 (522; 536)	512/546	51,1, 49,9	Screening 84 (7,9) Symptomatic 974 (92,1)	EndoScreener, Wision AI, Shanghai, China
Wang 2020	RCT, double-blinded, sham control	962 (484, 478)	495/467	49, 49	Screening 158 (16,4) or Symptomatic 804 (83,6)	EndoScreener, Wision AI, Shanghai, China; TensorRT, Nvidia, Santa Clara, CA, USA)
Gong 2020	RCT, single-blinded	704 (355; 349)	345/359	50, 49	Health examination 123 (17,5) Diagnostic 545 (77,4) Surveillance 36 (5,1)	ENDOANGEL, Wuhan University, Wuhan, China
Su 2020	RCT, single-blinded	623 (308; 315)	307/316	50,5; 51,6	Screening/surveillance 216 (34,7) Symptomatic 407 (65,3)	AQCS model, Jinan, China
Liu 2020	RCT, single-blinded	1026 (508; 518)	551/475	51; 50,1	Screening 66 (6,4) Symptomatic 960 (93,6)	CADe system, Henan Xuanweitang Medical Information Technology, Zhengzhou City, China
Total		4373 (2177; 2196)	2210/2163			

[Table 1: Characteristics of included studies]

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time automatic quality control system on colorectal polyp and adenoma detection: a prospective randomized controlled study (with videos). *Gastrointest Endosc* 2020; 91: 415-424.e4 Im 3. Liu W, et al. Study on detection rate of polyps and adenomas in artificial-intelligence-aided colonoscopy. *Saudi J Gastroenterol* 2020; 02: 2 Im 4. Wang P, et al. Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. *Gut* 2019; 68: 1813-1819 Im 5. Wang P, et al. Effect of a deep-learning computer-aided detection system on adenoma detection during colonoscopy (CADE-DB trial): a double-blind randomised study. *Lancet Gastroenterol Hepatol* 2020.

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ARTIFICIAL INTELLIGENCE-ASSISTED RECOGNITION OF CECAL INTUBATION

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Introduction: It is known that cecal intubation is an important quality indicator in colonoscopy (Rex DK, et al. GIE 2015). However, convincing cecal recognition can sometimes be difficult because of anatomic variations in the ileocecal valve (Rex DK. GIE 2000).

Aims & Methods: An artificial intelligence (AI) system was constructed by supervised learning. That is, we annotated whether the ileocecal valve was present or absent in every image. The image sequences containing the ileocecal valve were classed as cecal images and those that did not were treated as other images. We collected 27,193 endoscopic images (1,798 cecal images and 25,395 other images) from study participants who underwent colonoscopy performed using a CF-H290ECI (Olympus, Tokyo, Japan) from January 2016 to January 2020 at our institution for its learning. To train the AI, the annotated images were used to perform transfer learning on a pre-trained VGG16, which is one of the most common convolutional neural networks.

To evaluate its performance, we retrospectively collected colonoscopy images according to the following inclusion criteria: i) the colonoscopy was performed from January 2015 to June 2017 at our institution and ii) the images were recorded by a CF-HQ290ZI (Olympus, Tokyo, Japan). The exclusion criteria were i) advanced colon cancer invasion to the ileocecal valve and ii) poor quality image sequences.

The collected images were analyzed by the AI. The sensitivity, specificity, and accuracy of cecal image recognition were obtained.

Results: A total of 4,775 endoscopic test images (894 cecal images and 3,881 other images) were collected. The AI correctly recognized 782 out of 894 cecal images and 3,398 out of 3,881 other images. The sensitivity, specificity, and accuracy were 87.5%, 87.5%, and 88%, respectively.

Conclusion: In this pilot study, it was possible to automatically recognize the ileocecal valve with relatively good accuracy, despite the limited number of images. Although it will be necessary to improve accuracy by further training, this AI should be able to automatically record cecal intubation, which is an important quality indicator in colonoscopy.

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Disclosure: Nothing to disclose

P1235

ANALYSIS OF PREDICTIVE FACTORS FOR R0 RESECTION, IMMEDIATE BLEEDING AND RECURRENCE OF COLORECTAL ADENOMAS AFTER ENDOSCOPIC MUCOSAL RESECTION

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Introduction: Larger colonic polyps require advanced resection techniques such as endoscopic mucosal resection (EMR) for safe and effective removal. There has been a steady accumulation of scientific evidence with regards to the technical aspects and long-term outcomes of colonic EMR compared with surgery.

Aims & Methods: A retrospective cohort study was done on all patients who underwent colorectal EMR at the St. Luke's Medical Center Global City, Philippines within a 4-year period from 2015 to 2018. The study aims to determine the predictive factors of different clinical outcomes post-EMR namely R0 resection, complications and recurrence of colorectal adenomas. Secondary outcomes included the determination of the R0 resection rate, EMR-related complications, and recurrence rate of colorectal adenomas among patients who underwent colonic EMR. The study also aims to determine the diagnostic yield of JNET classification of the lesions in comparison to the histopathologic findings. Descriptive statistics was used to summarize the general and clinical characteristics of the participants. Odds ratio and the corresponding 95% confidence interval from logistic regression was computed to determine the association between patient profile and R0 resection according to en bloc resected, complication (bleeding or perforation), and resection statuses. Diagnostic accuracy tests were used to determine the sensitivity, specificity, predictive value and accuracy of the JNET classification in predicting appropriate histopathology.

Results: A total of 282 patients were studied. The mean age was 60 years with a male preponderance (57%). The most common technique employed was the conventional EMR (94%). Crudely, gross lesion size >20mm (cOR 16.375 [95% CI 1.965 to +Inf]), presence of submucosal fibrosis (cOR 15.617 [95% CI 1.22 to 132.98]), histopathologic size (cOR 1.1 [95% CI 1.01 to 1.19]), and diagnosis of moderately differentiated adenocarcinoma (cOR 225.106 [95% CI 17.11 to 14256.58]) were the factors associated with greater odds of having a positive resection margin among en bloc resection patients. The odds of immediate bleeding were increased with longer length of stay ($p = 0.008$), gross size >20mm (p value < 0.001), piecemeal resection ($p = 0.041$), and longer procedural duration ($p < 0.001$).

On crude analysis, the only factors associated with recurrence as per follow-up visit/s ($n=103$) were non-granular morphology (cOR 9.683 [95% CI 1.78 to 54.98]) and piecemeal resection (cOR 1.221 [95% CI 2.44 to 60.69]). The R0 resection rate is 96.3% for lesions resected en bloc. 15.2% had a complication, most commonly intraprocedural bleeding which were successfully managed endoscopically. 10.7% had recurrence post-EMR on their surveillance colonoscopy.

The JNET classification exhibited good sensitivity for Type 1 (71.8%) and Type 2A (91.9%) and good specificity for Type 1 (96.9%) and Type 2B (95.5%). Accuracy was high at 91.02% for Type 1, 80.24% for Type 2A and 89.22% for Type 2B.

Conclusion: EMR is an important advancement in the field of therapeutic endoscopy with good clinical outcomes sparing patients from surgery with a high R0 resection rate, low complication rate, and low recurrence rate. A larger lesion size of >20 mm is associated with both positive resection margin and post-EMR complications. Main predictors of recurrence include a non-granular morphology of a resected polyp and piecemeal resection. The JNET classification has a high diagnostic accuracy rate; hence is a good endoscopic tool for characterization of lesions.

Disclosure: Nothing to disclose

P1236

VALIDATION STUDY TO DIAGNOSE THE DEGREE OF SUBMUCOSAL CANCER INVASION IN COLORECTAL ESD

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Introduction: The possibility of complete curative en bloc resection for colorectal T1 cancer is sometimes related to the degree of the submucosal (SM) cancer invasion. In this study, we performed the validation study of ESD cases for colorectal T1 cancers accompanied by fibrosis.

Aims & Methods: The aim of this study was thus to complete R0 resection for colorectal T1 cancers showing fibrosis in the SM layer. The subjects were 121 T1 cancers in 121 patients (male 61, female 60, average 67.8 years old) during 1,685 lesions in 1,644 patients performed colorectal ESD. All these cases had a diagnosis of T1 cancer by postoperative pathological diagnosis. In cases with cancer invasion, endoscopic findings of the fibrotic area showed a whitish or brownish hump with rich abnormal vessels associated with caliber change and uneven distribution. The ESD cases were classified in three groups from the viewpoint of fibrosis: absence of fibrosis (A), fibrosis due to benign causes (B), and fibrosis due to cancer invasion (C).

Furthermore, cases were classified as mild (grade 1), moderate (grade 2), or severe (grade 3). In this study, we examined the following items. (1) Validation study on the ability for differential diagnosis of cancerous fibrosis and noncancerous benign ($n=146$) was performed during ESD procedure. (2) The depth of submucosal cancer invasion was measured using a micrometer and compared in Type C lesions. (3) Comparisons of the en bloc resection rate and R0 rate of Type C-1, C-2, and C-3.

Results: The macroscopic configurations of the 121 cases were forty one 0-Is+IIa type cases, forty 0-IIa type cases, twenty 0-Is type cases, twelve 0-IIa+IIc type cases, and eight 0-IIc type cases. The average lesion size was 33.8 mm (15-110 mm) in diameter. (1) As the results of the validation study ($n=267$) for differential diagnosis between Types C and B as follows; sensitivity: 81.8%, specificity: 93.8%, accuracy: 91.7%, PPV: 91.7%, NPV: 86.2%. (2) The depth of SM cancer invasion of Type C resulted in the following: Type C-1 ($n=67$); $801.2 \pm 956.1 \mu\text{m}$; Type C-2 ($n=28$) $1745.0 \pm 891.6 \mu\text{m}$; and Type C-3 ($n=26$) $3063.5 \pm 2008.4 \mu\text{m}$.

Also, we recognized a significant difference ($p < 0.01$) statistically between each group. (3) The accuracy rate, an en bloc resection rate, and R0 rate of each group of Type C were as follows: Type C-1; accuracy: 74.6%, en bloc: 98.5%, R0: 97.0%, Type C-2; accuracy: 92.9%, en bloc: 92.9%, R0: 82.1%, Type C-3; accuracy: 92.9%, en bloc: 69.2%, R0: 34.6%. 88.8%; B-3: 63.3%; Type C-1: 100%; C-2: 91.4%; C-3: 61.5%. The en bloc resection rate and R0 rate for Type C-3 were significantly lower ($P < 0.01$) than that for Type C-1 and C-2. Also, withdrawn cases were significantly higher (7/26:26.9%, $P < 0.01$) in Types C-3 compared with Type C-1 and C-2. Whereas the accuracy rate of Type C-2 and C-3 were superior to Type C-1.

From these results, T1 cancers accompanied by mild to moderate fibrosis become the standard indication for ESD. Whereas Type C-3 lesions accompanied by severe fibrosis with the retraction of proper muscle should be indicated as additional radical operation.

Conclusion: Accurate diagnosis of fibrosis accompanied by submucosal cancer invasion during ESD appears feasible and contributes to completing R0 resection for colorectal T1 cancers.

Disclosure: Nothing to disclose

P1237

DYE-BASED CHROMOENDOSCOPY VERSUS STANDARD-DEFINITION AND HIGH-DEFINITION WHITE LIGHT ENDOSCOPY FOR ADENOMA DETECTION IN PATIENTS WITH LYNCH SYNDROME: META-ANALYSIS OF INDIVIDUAL PATIENT DATA FROM RANDOMISED TRIALS

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Introduction: The additional diagnostic value of dye-based chromoendoscopy (CE) compared to standard and high-definition white-light endoscopy (SD-WLE and HD-WLE) for surveillance of Lynch syndrome patients is subject to debate.

Aims & Methods: To clarify this debate, an individual patient data meta-analysis was performed according to the PRISMA-IPD guidelines. Randomised controlled trials comparing the efficacy of dye-based CE to WLE (SD and HD) for the detection of adenomas in Lynch patients were included. Only individuals with a proven Lynch syndrome associated gene mutation (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *EpCAM*) were included.

The primary outcome measure was the adenoma detection rate (i.e. proportion of patients with at least one adenoma detected during colonoscopy). Patients were subdivided in two groups: (1) SD equipment and (2) HD equipment.

Mixed-effect logistic regression models were used to estimate the adenoma detection rate across studies. To account for heterogeneity between-trials random intercept for study was used.

Results: Two randomised controlled trials and one randomised colonoscopy tandem study were included, comprising 533 Lynch syndrome patients with a proven gene mutation. The mean age of patients was 46 years (SD 13) and 218 (44%) were male. Baseline characteristics of the included patients did not differ between CE and WLE. HD equipment was used in 363/533 (68%) of the colonoscopy procedures. The adenoma detection rate was 74/265 (28%) in patients randomised to WLE compared to 83/266 (31%) patients randomised to CE (odds ratio [OR] 1.17; 95% CI 0.81-1.70, $P=0.41$).

There was no difference in adenoma detection rate for either imaging modality within the HD equipment group (OR 1.20, 95% CI 0.77-1.90, $p=0.42$) or the SD equipment group (OR 1.17; 95% CI 0.60-2.32, $P=0.65$). The mean number of adenomas per patient detected with CE was 0.52 compared to 0.47 with WLE (incidence rate ratio [IRR] 1.09; 95%CI 0.78-1.52, $P=0.60$). Subgroup analyses showed no significant differences between CE and WLE for proximal adenomas (OR 1.40, 95%CI 0.92-2.14, $P=0.11$), flat adenomas (OR 1.34; 95%CI 0.80-2.24, $P=0.26$) or diminutive adenomas (OR 1.21, 95%CI 0.81-1.81, $P=0.34$). CE was more time consuming than WLE with a mean extubation time of 19 minutes for CE versus 12 minutes for WLE ($P<0.01$).

Conclusion: In this meta-analysis of individual Lynch syndrome patients in randomised controlled trials, dye-based CE did not increase the adenoma detection rate compared to SD-WLE and HD-WLE. As dye-based CE was associated with a prolonged extubation time and recent studies show that HD equipment correlates with an increased adenoma detection¹, we recommend the use of HD-WLE as the preferred imaging modality for the surveillance of patients with Lynch syndrome.

Equipment	N. studies	WLE % (n/N)	CE % (n/N)	Odds ratio* (95% CI)	P-value
All	3	27.9% (74/265)	31.2% (83/266)	1.17 (0.81-1.70)	0.42
Standard-definition	2	29.5% (23/78)	32.9% (25/76)	1.17 (0.59-2.32)	0.65
High-definition	2	27.0% (74/178)	30.8% (57/185)	1.21 (0.77-1.90)	0.42

[Analysis results for the adenoma detection rate. * Calculated as odds of adenoma detection in CE group relative to odds in WLE group]

*The colon of p]

References: 1. Tziatzios G, Gkolfakis P, Lazaridis LD, et al. High-definition colonoscopy for improving adenoma detection: a systematic review and meta-analysis of randomized controlled studies. *Gastrointest Endosc* 2020.

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P1238

CHARACTERISTICS OF DEPRESSED TYPE COLORECTAL NEOPLASMS IN MAGNIFYING ENDOSCOPY AND ENDOCYTOSCOPY

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Introduction: Colorectal cancers are generally recognized to develop from “polyps”. This “adenoma-carcinoma sequence” theory has been in the mainstream of development of colorectal cancers. However, recently the existence of many depressed-type cancers has been revealed, which are considered to emerge directly from normal epithelium, not through the adenomatous stage. This theory is called “de novo” pathway.

Now, it is possible to presume the histology of colorectal lesions using magnifying endoscopy (pit pattern classification) and endocytoscopy (EC classification). We can observe not only the structural atypia but also the cellular atypia in vivo.

Aims & Methods: The aim is to clarify the endoscopic characteristics of depressed-type colorectal neoplasms, demonstrating the validity of pit pattern and EC classification.

A total of 37134 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our unit from April 2001 to December 2019. Of these, 29413 lesions were low-grade dysplasia, 6391 were high-grade dysplasia and 1330 were submucosally invasive (T1) carcinomas. According to the developmental morphology classification, they were divided into 3 types: depressed, flat and protruded-type. We investigated the rate of T1 carcinomas and the characteristics of depressed-type neoplasms concerning pit pattern and EC classification.

Results: The rate of T1 carcinomas in depressed-type lesions reached to 62.5%, meanwhile that in flat-type and protruded-type lesions was 2.8% and 2.7%, respectively. Within less than 5mm in diameter, that was 10%, 0.01% and 0%, respectively. Most of the flat-type (91.5%) and protruded-type (94.9%) lesions showed type III_L or IV pit pattern corresponding to adenomas, whereas 92.2% of the depressed-type lesions were characterized by type III_S, V_I or V_N pit patterns corresponding to carcinomas. As for endocytoscopy, most of the flat-and protruded-type lesions showed EC2 corresponding to adenomas. In contrast, the depressed-type lesions were observed as EC3a (37.0%) and EC3b (55.6%) corresponding to invasive carcinomas.

Conclusion: This study revealed the diagnostic characteristics of depressed-type lesions. They show typically type III_S, V_I or V_N pit patterns in magnifying endoscopy and type EC3a or EC3b in endocytoscopy. These lesions tend to invade the submucosal layer even when they are small. It is important to diagnose colorectal neoplasms according to their morphology.

Disclosure: Nothing to disclose

P1239

IMPACT OF LESION PHENOTYPE ON COLORECTAL CANCER MORTALITY AND OVERALL MORTALITY: INSIGHTS FROM A NATIONWIDE SCREENING COLONOSCOPY PROGRAM

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Introduction: The long-term risk of colorectal cancer (CRC) mortality and overall mortality after screening colonoscopy is poorly investigated. Most studies analyzed mixed cohorts of screening individuals, and symptomatic or individuals with positive fecal immunohistochemical testing.

Aims & Methods: We aimed to analyze CRC mortality and overall mortality after screening colonoscopy by lesion phenotype. Screening colonoscopies performed within the quality assurance program in Austria between 11/2007 and 06/2018 were matched with a national mortality register. The following lesion phenotypes were defined:

- 1) negative colonoscopy,
- 2) low-risk adenoma,
- 3) high-risk adenoma,
- 4) hyperplastic polyps, and;
- 5) serrated lesions.

Age and sex adjusted Cox regression analyses were used to analyze the association between lesion phenotypes, CRC mortality and overall mortality.

Results: 280,291 screening colonoscopies were included in the study. 7,311 deaths of any cause occurred after 55±35.6 months of follow-up, 4,730 men and 2,581 women. Overall mortality rates, adjusted for age and sex, were significantly higher for individuals with high-risk adenomas (HR 1.6, 95%CI 1.5-1.7, p< 0.01), low-risk adenomas (HR 1.1, 95%CI 1.0-1.7, p=0.006), and hyperplastic polyps (HR 1.1, 95%CI 1.0-1.2, p=0.004), but not for serrated lesions (HR 1.2, 95%CI 1.0-1.5, p=0.083), compared to negative colonoscopy.

Among a total of 232 CRC deaths (ICD 10: C19-21), 156 were observed in men and 76 in women. High-risk adenomas (HR 8.9, 95%CI 6.5-12.1, p< 0.001) and serrated lesions (HR 4.3, 95%CI 1.9-10.0, p=0.001), but not for low-risk lesions (HR 1.3, 95%CI 0.8-2.1, p=0.350) and hyperplastic polyps (HR 1.5, 95%CI 0.9-2.4, p=0.138) were at higher risk for CRC death as compared to negative colonoscopy.

Conclusion: In individuals undergoing screening colonoscopy, the lesion phenotype is significantly associated with both CRC-related and all-cause mortality.

Disclosure: Nothing to disclose

P1240

IS THERE STILL A PLACE FOR FLEXIBLE SIGMOIDOSCOPY IN THE "FIT" ERA?

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Introduction: Flexible sigmoidoscopy continues to be used for left sided colonic symptoms to exclude colorectal cancer distal to the splenic flexure. Usage in symptomatic patients has been on the wane with more sensitive stool tests, investment in colorectal services and advances in radiology. We sought to quantify post-flexible sigmoidoscopy colorectal cancer rates in symptomatic patients to determine the diagnostic yield for colorectal cancer (CRC) and provide quality assurance.

Aims & Methods: We performed a retrospective review of all flexible sigmoidoscopies for symptomatic patients between March 2010 and March 2016. We used cancer registry data to identify all patients with CRC who had had a negative flexible sigmoidoscopy in the preceding 3 years.

Patients who were diagnosed within 6 months were excluded to allow for time for linkages between databases and complexity delaying the diagnosis to avoid inappropriately misclassifying patients.

Flexible sigmoidoscopies were categorised as true positive (CRC within 6 months of the index procedure) and false negative (CRC within 6-36 months). We performed a qualitative review of each false negative.

Results: 7199 flexible sigmoidoscopies were done over 6 years. 232 (3.2%) cases of CRC were diagnosed at index test (true positives). The false negative rate was 3.75% (9/240). The false negative rate was higher in women at 6.1% (6/99) vs 2.12% (3/141) in men. There were no false negatives in individuals younger than 60 years. The false negative rate in those over 60 was 4.6% (9/194).

All but 2 of the false negative cases were proximal to the splenic flexure, 1 was beyond the extent of the flexible sigmoidoscopy, the other within a diverticular segment which had been passed. 6/9 had an indication for full colonic review. 2 had iron deficiency anaemia, 1 had a change in bowel with loss of weight and 3 had undiagnosed abdominal pain. In hindsight, it is likely that the missed cancer explained the symptoms. It is acknowledged that the indications were of variable strength.

Conclusion: Advancing age and female gender are associated with higher false negative rates. Bowel preparation was not a factor in missed CRC. Our data suggest that flexible sigmoidoscopy is a safe first line test in patients with left sided colonic symptoms to exclude colorectal cancer given the low false negative rate. Furthermore, the diagnostic yield was similar to other invasive investigations for alarm symptoms. However, adequate consideration of complex symptoms is essential to ensure there are no indications for a full colonoscopy.

Disclosure: Nothing to disclose

P1241 WITHDRAWN

P1242

NUCLEAR OBSERVATION WITH ENDOCYTOSCOPY PROVIDES ADDITIONAL DIAGNOSTIC ABILITY TO PIT PATTERN FOR ULCERATIVE COLITIS ASSOCIATED NEOPLASIA

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Introduction: With the recent proposal of a target biopsy protocol of surveillance colonoscopy for ulcerative colitis associated neoplasia (UCAN), optical biopsy with advanced endoscopic techniques have attracted attention. Pit pattern (PIT) is efficacious but remains an important unmet need because inflammation changes the mucosa, which is sometimes diagnosed as neoplastic PIT; low specificity. Endocytoscopy (EC), at ×520 magnification, allows visualization of cell nuclei.

Aims & Methods: The aim of this retrospective study was to evaluate the clinical efficacy of a novel strategy consisting of EC irregular formed nuclei combined with PIT to predict UCAN. This study involved patients with ulcerative colitis, whose lesions were observed with EC in a referral hospital between February 2007 and April 2020. Each lesion was initially diagnosed with PIT followed by EC diagnosis by two independent expert endoscopists. The diagnostic abilities of PIT alone and PIT plus EC irregular formed nuclei to predict UCAN were compared. We also examined the difference in the diagnostic abilities of PIT plus EC according to endoscopic inflammation severity using the Mayo endoscopic score (MES).

Results: Overall, 103 lesions from 62 patients were analyzed: 23 lesions were UCAN and 80 were non-neoplastic. In PIT plus EC diagnosis, the sensitivity, specificity, and accuracy were 100% (23/23, 78.9%-100%), 87.5% (70/80, 78.2%-93.8%), and 90.3% (93/103, 82.9%-95.2%) by evaluator 1; 100% (23/23, 78.9%-100%), 81.2% (65/80, 71.0%-89.1%), and 85.4% (88/103, 77.1%-91.6%) by evaluator 2. Results from both evaluators indicated PIT plus EC had a significantly higher specificity, and accuracy compared with PIT: 87.5% (70/80, 78.2%-93.8%) versus 58.8% (47/80, 47.2%-69.6%) (P < 0.01), and 90.3% (93/103, 82.9%-95.2%) versus 67.0% (69/103, 57.0%-75.9%) (P < 0.01) for specificity, and accuracy, respectively, by evaluator 1; 81.2% (65/80, 71.0%-89.1%) versus 56.2% (45/80, 44.7%-67.3%) (P < 0.01), and 85.4% (88/103, 77.1%-91.6%) versus 66.0% (68/103, 56.0%-75.1%) (P < 0.01) for specificity, and accuracy, respectively, by evaluator 2.

	PIT alone: % (95% CI)	PIT plus EC: % (95% CI)	P value
Evaluator 1	-	-	-
Sensitivity	95.7 (78.1-99.9)	100 (78.9-100)	1
Specificity	58.8 (47.2-69.6)	87.5 (78.2-93.8)	< 0.01
Accuracy	67.0 (57.0-75.9)	90.3 (82.9-95.2)	< 0.01
Evaluator 2	-	-	-
Sensitivity	100 (78.9-100)	100 (78.9-100)	1
Specificity	56.2 (44.7-67.3)	81.2 (71.0-89.1)	< 0.01
Accuracy	66.0 (56.0-75.1)	85.4 (77.1-91.6)	< 0.01

[The diagnostic values of EC plus PIT compared with PIT alone to predict UCAN.]

Regarding differences in the diagnostic ability according to MES, the accuracy and specificity were higher for an MES of 0-1 than an MES of 2-3; 97.1% (67/69, 89.9%-99.6%) versus 76.5% (26/34, 58.8%-89.3%) (P < 0.01),

and 96.2% (50/52, 86.8%-99.5%) versus 71.4% (20/28, 51.3%-86.8%) ($P < 0.01$), for accuracy and specificity, respectively, by evaluator 1; 92.8% (64/69, 83.9%-97.6%) versus 70.6% (24/34, 52.5%-84.9%) ($P < 0.01$), and 90.4% (47/52, 79.0%-96.8%) versus 64.3% (18/28, 44.1%-81.4%) ($P < 0.01$), for accuracy and specificity, respectively, by evaluator 2.

Conclusion: Our novel strategy using PIT plus EC irregular formed nuclei had a higher diagnostic ability to predict UCAN compared with PIT alone.

Disclosure: Nothing to disclose

P1243

THE GOBLET APPEARANCE OBSERVED WITH ENDOCYTOSCOPY FOR PREDICTION OF HISTOLOGICAL MUCIN DEPLETION AND CLINICAL RELAPSE IN PATIENTS WITH ULCERATIVE COLITIS MAYO ENDOSCOPIC SCORE OF 0

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Introduction: With a Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) program, a Mayo endoscopic score (MES) of 0 was recommended as the optimal target in the management of ulcerative colitis (UC)¹. However, some patients clinically relapse in the short term despite a MES of 0 was achieved. Recently, it has been reported that the histological mucin depletion was an independent clinically relapse factor of patients with a MES of 0².

Aims & Methods: The aim of this single-center retrospective study was to evaluate clinical efficacy of the goblet appearance observed with endocytoscopy (EC: $\times 520$ ultra-magnifying colonoscopy). This study was performed in two phases - i) the correlation between the EC goblet appearance and the histological mucin depletion severity, and ii) the correlation between the EC goblet appearance and the clinically relapse. i) the subjects were including all UC patients who were taken a biopsy sample from rectum, after EC observation at the target area between October and November 2018. The numbers of goblet appearance in each EC image were counted by an endoscopist who was blinded to clinical, histological, and endoscopic information. An expert pathologist classified biopsy samples into three groups according to severity of mucin depletion. the correlation between the goblet appearance and the histological mucin depletion severity was assessed. ii) the study cohorts were including previously established UC patients in sustained corticosteroid-free (≥ 6 months) clinical remission (defined as partial Mayo score of ≤ 1) and a MES of 0 undergoing endoscopic evaluation using EC between October 2016 and December 2019. Exclusion criteria was the patients who became pregnancy or were undergone surgery under general anesthesia during the follow-up period.

Subsequently, we classified patients into the smaller number group or the larger number group; the smaller number group as patients with the number of EC goblet appearances ≤ 86 , and the larger number group with the number of EC goblet appearances ≥ 87 . Cohorts were followed until the end of the study in May 2020 or until relapse. Clinical relapse was defined as a partial mayo score ≥ 3 or the presence of rectal bleeding together with any treatment intervention. The main outcome measure was the difference in clinical relapse-free rates between the two groups.

Results: i) A total of 16 patients were included as the study subject. There was a negative correlation with the Spearman correlation coefficient of -0.797 . between the number of EC goblet appearance and the histological goblet mucin depletion severity. ii) A total of 110 patients were included as the study cohort. We classified 74 patients into the smaller number group and 36 into the larger number group. The mean follow-up period was 487 days. The mean number of EC goblet appearances in non-relapsed patients (83.9) was significantly lower than that in relapsed patients (39.0) (T-test, $P=0.01$).

The ratio of clinically relapse in the larger goblet appearance number group was 2.8% (1/36), while that in the smaller number group was 13.5%(10/74), respectively. The larger number group had a significantly higher clinical relapse-free rate compared with the smaller number group (Log-rank test, $P=0.04$).

Conclusion: The EC goblet appearance has a potential to predict both histological mucin depletion and clinically relapse in patients with a MES of 0.

References: 1) Peyrin-Biroulet L, et al. Am J Gastroenterol. 2015; 110(9): 1324-38. 2) Ozaki R, et al. Journal of Crohn's and Colitis. 2018; 12:1288-94.

Disclosure: Nothing to disclose

P1244 WITHDRAWN

P1245

EFFECTIVENESS AND TOLERABILITY OF 1L PEG-ASC PREPARATION FOR COLONOSCOPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: The effectiveness of bowel cleansing is a key element for a quality colonoscopy, especially for a proper evaluation of the endoscopic outcomes in patients with inflammatory bowel disease (IBD). Recently, a very-low-volume 1L PEG-ASC solution (Plenvu®; Norgine, Harefield, UK) has been introduced. Nevertheless, the effectiveness and safety of this preparation in IBD patients have not been assessed.

Aims & Methods: This study aimed to evaluate the effectiveness, tolerability and safety of 1L PEG-ASC preparation in patients with IBD compared to controls.

We retrospectively reviewed a prospective cohort of 411 in- and out-patients aged >18 years performing a colonoscopy, after an afternoon/morning or a same-day 1L PEG-ASC preparation consecutively enrolled from November 2019 to February 2020 in 5 Italian centres. Bowel cleansing was assessed through the Boston Bowel Preparation Scale (BBPS), a bowel cleansing success was defined as a total BBPS ≥ 6 with a partial BBPS ≥ 2 in each colon segment and a high-quality cleansing of the right colon as a partial BBPS=3. Tolerability was evaluated through a semi-quantitative scale with a score ranging from 0 to 10. Safety was monitored through adverse event (AE) reporting.

Results: All 411 patients were included in the analysis. Among these, 185/411 (45%) were IBD patients (51.4% with Ulcerative Colitis [UC] and 48.6% with Crohn's Disease [CD]) and 226/411 (55%) controls.

Overall, mean age was 47.4 ± 15.1 and 59.9 ± 15.6 , males were 58.4% and 51.8% and prevalence of comorbidities 31.9% and 34.5% in the IBD and the control group respectively.

Patients UC with had extensive colitis, left-sided colitis and proctitis in 51.6%, 34.7% and 13.7% of cases, respectively, while the average partial Mayo score was 2.0 ± 2.2 , and the mean disease duration 11.7 ± 8.6 years.

Patients with CD had an ileal, ileocolic and colic localization of disease in 54.5%, 26.1% and 19.3% of cases, respectively, while the mean Harvey Bradshaw index was 3.0 ± 2.6 and the mean disease duration 9.5 ± 6.3 years. Overall, bowel cleansing by BBPS was 7.5 ± 1.3 and 7.3 ± 1.4 ($p=0.2$) while the right colon cleansing was 2.3 ± 0.5 and 2.3 ± 0.6 ($p=0.8$) in IBD and control group, respectively. A significantly higher bowel cleansing success was achieved in patients with IBD (92.9% vs 85.4%, $p=0.02$), with a similar high-quality cleansing of the right colon (39.1% vs 40.5%, $p=0.7$) compared to controls. Tolerability between the two groups was similar with an average tolerability score of 7.5 ± 1.2 vs 7.7 ± 1.4 ($p=0.1$) respectively.

The number of patients with any mild to moderate treatment-related adverse events (AEs) was lower in the IBD compared to the control group (8.6% vs 22.1%, $p<0.001$), with a different distribution of AEs.

In the IBD group, compared to controls, a significantly lower incidence of vomit (1.6 vs 5.8%, $p=0.03$), and a significantly higher incidence of abdominal pain (8.6 vs 0.4%, $p<0.01$) probably also secondary to the presence of the bowel disease, were registered, with a similar incidence of hypotension (0.5 vs 1.8%, $p=0.2$) and dehydration (1.1 vs 1.3%, $p=0.8$). No severe AEs occurred in any of the two groups.

Conclusion: This study shows that 1L PEG-ASC solution (Plenvu®) has high effectiveness in IBD patients, with similar tolerability compared to controls, and a good safety profile. The high overall success rates achieved with this preparation may, therefore, contribute to a more accurate definition of endoscopic outcomes in IBD patients.

Disclosure: Nothing to disclose

P1246

THE INFLUENCE OF “BIOPSY RELATED FACTORS” ON THE NON-LIFTING SIGN IN COLORECTAL LATERALLY SPREADING TUMOR

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Introduction: For colorectal laterally spreading tumor (LST), endoscopic removal is now recognized as first-line therapy internationally. However, The problem of biopsy before endoscopic treatment has always troubled clinicians. In any case, about 50% of lesions would undergo a preceding biopsy in clinical operations. This study aimed to explore the impact of preoperative biopsy and other factors on the non-lifting sign, and further explored the influence of “biopsy related factors” such as number of biopsy specimen and the interval after biopsy on non-lifting sign in cases with a history of biopsy.

Aims & Methods: Clinical data of 159 LSTs were reviewed from the endoscopic system and case system retrospectively. Details regarding age, gender, history of biopsy, tumor location, tumor size, the depth of submucosal invasion, tumor configuration according to the Kudo classification and Paris classification, histologic type, and location with respect to the fold were investigated. For patients with a history of biopsy, the period between the biopsy and non-lifting sign testing, number of biopsy specimen, age, gender, tumor location, tumor size, SM depth, tumor configuration according to the Kudo classification and Paris classification, histologic type, and location with respect to the fold was analysis.

Results: A total of 159 LST cases were tested for lifting signs, in which the results of 112 cases were positive for lifting signs and 47 were negative. The incidence of the non-lifting sign was significantly higher in lesions ≥ 30 mm than < 30 mm ($P=0.003$). Lesions with a history of biopsy exhibited the non-lifting sign more frequently than those without a history ($P=0.002$). In addition, location with respect to the fold and pathological type were also significantly associated with the non-lifting sign ($P=0.028$ and 0.002 respectively). A history of biopsy ($P=0.008$), tumor size ($P=0.010$) and location with respect to the fold ($P=0.022$) were identified as factors affecting the non-lifting sign in multivariate analyses.

In 75 LST cases with a history of biopsy, the incidence of the non-lifting sign was significantly higher in lesions with size ≥ 30 mm than < 30 mm ($P=0.005$). The average number of biopsy specimen in the lifting sign positive group was 1.47 and 2.86 in the negative group ($P<0.001$). Patients with a history of biopsy of more than one specimen exhibited the non-lifting sign more frequently than those with only one specimen, and the difference was significant too ($P<0.001$). Only the number of biopsy ($P=0.003$) was identified as a factor affecting the non-lifting sign in multivariate analyses. **Conclusion:** For LST, lesions with larger size, being across the fold, and biopsy history were predictive factors for non-lifting signs. Reducing the number of biopsies would reduce the occurrence of non-lifting signs when biopsy was necessary. The Paris and Kudo classification of LST had no obvious predictive value. The impact of the interval after the biopsy on the non-lifting sign required further study.

Disclosure: Nothing to disclose

P1247

EC-V (ENDOCYTOSCOPIC VASCULAR) CLASSIFICATION IS USEFUL FOR NOT ONLY QUALITATIVE DIAGNOSIS BUT ALSO PATHOLOGICAL DIAGNOSIS

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Introduction: Endocytoscopy (EC) is a new device launched in 2019 whose focus depth is 50µm. EC allows visualization of the glandular structure and cellular atypia *in vivo*.

Thus far, narrow-band imaging (NBI) could make it possible to analyze the surface microvessels of colorectal lesions for differentiating neoplasms from non-neoplasms and for predicting the histopathological diagnosis. Using EC with NBI (EC-NBI), it enables *in vivo* observation of blood vessels in more detail compared to conventional magnification power without the use of any dye solution.

Aims & Methods: The aim of this study was to validate the evidence whether the observation of surface microvessels using EC-NBI was useful in predicting the histopathology of colorectal lesions.

The study included 622 patients who underwent complete colonoscopy and endoscopic or surgical treatment between April 2006 and December 2019. A total of 997 lesions (118 Non-neoplastic polyps, 640 adenomas, 77 intramucosal cancer(M), 21 slightly invasive submucosal cancer (SMs) and 141 massively invasive submucosal cancer(SMm)) were retrospectively evaluated. We used the Kudo classification for the degree of submucosal invasion. SMs cancer without vessel permeation does not metastasize. In contrast, SMm lesions show a substantial proportion (~10%) of lymph node metastasis. We named the ultra-magnified microvessel findings as EC-V classification and classified into the following 3 groups: EC-V1, the

surface microvessels were very fine obscure; EC-V2, the surface microvessels were more clearly seen and showed a regular vessel network, and their caliber and arrangement were uniform; and EC-V3, the surface microvessels were thick, and their caliber and arrangement were non-homogeneous. The main pathologies of EC-V1, EC-V2, EC-V3 were hyperplastic, adenoma, SMm, respectively.

Results: The sensitivity, specificity and accuracy of EC-V1 for diagnosis of hyperplastic polyp were 87.2%, 98.6% and 97.3%, respectively. Secondly the sensitivity, specificity and accuracy of EC-V2 for diagnosis of adenoma or M or SMs were 97.2%, 84.6% and 93.9%, respectively. Similarly the sensitivity, specificity and accuracy of EC-V3 for diagnosis of SMm were 82.3%, 98.9% and 96.6%, respectively.

Conclusion: EC-V classification was useful for predicting the histopathology of colorectal lesions.

Disclosure: Nothing to disclose

P1248

SCORING OF HISTOLOGICAL REMISSION IN ULCERATIVE COLITIS BASED ON AUTOMATED COMPUTER-AIDED ANALYSIS OF ENDOSCOPIC IMAGES OUTPERFORMS HUMAN SCORING

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Introduction: With the advent of magnifying endoscopy and specific illumination techniques more detailed images are available, with real-time endoscopic visualisation of histological structures. Changes in pericryptal vascular structures are associated with histological disease activity in ulcerative colitis (UC). Given the known inter- and intra-observer variability in central reading, computer-aided automated analysis may contribute to more objective scoring of histologic remission.

Aims & Methods: We compared the performance of an automated computer-aided image analysis technique to a human evaluation for scoring histological remission in UC.

Endoscopic images were prospectively collected in patients with UC. Images were taken with 3 image modalities: white light images (WLI), blue light images (BLI) and monochromatic short wavelength images (MLI) with a routine and magnifying scope. MLI enables to evaluate in real-time the superficial (< 200µm) mucosal architecture of the colonic wall. The computer-aided image analysis technique incorporated features extraction techniques, including pattern recognition of bleeding areas and high-density measurement of capillary structures, in still images. All images were randomly evaluated by 9 blinded endoscopists (4 senior, 5 junior) after a formal training session. The still images were assessed for histological remission: both a binary score (yes/no) and a visual analogue scale (VAS) in the 3 different illumination modes. The median score of all endoscopists was used to assess the performance. The histological score was derived from biopsies in the area of the corresponding images. Histological remission was defined as Geboes score < 2B.1. Inter-rater agreement was assessed with Kappa statistics and intraclass correlation coefficient. In addition, the Mayo endoscopic subscore (MES) and ulcerative colitis endoscopic index of severity (UCEIS) were scored based on video fragments.

Results: Two hundred thirteen endoscopic images (95 rectum, 81 sigmoid, 37 descending colon) were prospectively collected in 49 patients with UC. There was a low to moderate inter-rater agreement for UCEIS ($\kappa=0.31$)

and MES ($\kappa=0.46$) for all endoscopists. The junior endoscopists had lower agreement for UCEIS ($\kappa=0.29$ vs 0.36) and higher for MES ($\kappa=0.49$ vs 0.46) compared to the senior endoscopists. The inter-rater agreement for histological remission (yes/no) in all modes based on all endoscopists was low, with $\kappa=0.38$; 0.35; 0.30 for WLI; BLI; MLI respectively. Senior endoscopists had higher agreement (WLI $\kappa=0.44$ vs 0.32; BLI $\kappa=0.49$ vs 0.21; MLI: $\kappa=0.35$ vs 0.22) compared to junior. Agreement for remission VAS score was moderate to good between all endoscopist (WLI 0.76; BLI 0.83; MLI 0.73).

The performance of the human interpretation of histological remission was highest for WLI (table). The computer-based analysis of histological remission outperformed the human scoring in all modalities with a sensitivity of 0.84 and a specificity of 0.73 leading to an accuracy of 79%.

Illumination mode	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy overall	Positive likelihood ratio	Negative likelihood ratio
White light image	0.89	0.65	0.57	0.92	0.73	2.54	0.17
Blue light image	0.78	0.63	0.37	0.91	0.66	2.11	0.35
Monochromatic light image	0.77	0.51	0.23	0.92	0.55	1.57	0.45
Computer-aided analysis	0.84	0.73	0.73	0.85	0.79	3.11	0.22

[Performance of the computer aided analysis compared to human scoring]

Conclusion: Standard endoscopic scoring and scoring of histological remission in different imaging modalities in UC is prone to high inter-rater variability. Computer-aided analysis has no variability and outperforms human scoring. For this, the evaluation of advanced detailed endoscopic images is preferentially done by validated computer-aided analysis.

Disclosure: PB consultancy fees from Pentax; RB consultancy fees from Pentax

P1249

THE FEASIBILITY OF A FULLY SYNTHETIC AND SELF-ASSEMBLED PEPTIDE SOLUTION AS SUBMUCOSAL INJECTION MATERIAL: A PRELIMINARY STUDY

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Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are endoscopic resection techniques that can remove gastrointestinal adenomas and early-stage cancers. However, procedure-related complications such as bleeding and perforation may occur at a certain frequency. Submucosal injection is important to achieve good outcomes and reduce complications.

We hypothesized that the fully synthetic and self-assembled peptide (FSSP) solution, which is changed into a gel formed of nanofibers in contract with neutral pH environments creates a suitable submucosal cushion and makes endoscopic procedure safer. However, there is no evidence if this solution could be a potential submucosal injection material during endoscopic resection.

Aims & Methods: The aim of this study was to clarify the safety and efficacy of FSSP solution as a submucosal injection material. To compare the lesion-lifting properties, 1ml of 0.3% FSSP solution, Eleview[®], Sodium Hy-

aluronate solution (SHA) and normal saline (NS) were injected using a 23G injection needle into the submucosal layer of the stomach and colon in five live dogs under the general anesthesia. Their abdomens were opened and the mucosal surfaces of the stomach and colon were exposed by incision. The height and volume of submucosal cushion were measured with a digital caliper immediately and 10, 20, 30, and 40 minutes after injecting each solution. The sample experiment was repeated ten times for each solution in a blind fashion. We also evaluated histopathological findings at all injection sites using the grading system for assessment of tissue damage which was conceived based on histological findings such as inflammation, hemorrhage and edema.

Results: In the colon, there were significantly different trends among solutions in the stomach ($p=0.0096$, ANOVA for repeated measures). FSSP solution created significantly higher submucosal cushion than NS 20 minutes after injection ($p=0.0015$) and Eleview[®], and NS 40 minutes after injection ($p=0.0009$ and $p=0.0002$, respectively). FSSP solution also created significantly larger submucosal cushion than NS 20 and 40 minutes after injection ($p=0.0017$ and $p=0.015$, respectively). Furthermore, FSSP solution and SHA tended to maintain height and volume than other two solutions.

In the stomach, there were no significantly different trends among any of the graphs in the stomach ($p=0.25006$, ANOVA for repeated measures). However, FSSP solution created significantly higher submucosal cushions than by NS 40 minutes ($p=0.0059$). FSSP solution and SHA tended to maintain height and volume than other two solutions.

Histopathological assessments revealed that there was submucosal hemorrhage and edema at injection sites of all materials in the colon and stomach. Hematoma and slight necrosis were observed at one injection site of FSSP solution in the stomach. However, the grading scale of tissue damage by FSSP solution was not inferior compared to that by other solutions.

Conclusion: FSSP solution can create high and long-lasting submucosal cushion, which suggested that FSSP solution could be a safe and suitable material for endoscopic resection especially in the colorectum.

Disclosure: Toshio Uraoka received research fund from 3D Matrix Ltd.

P1250

ADVERSE EVENTS AND MORTALITY OF COLONOSCOPY IN AN ITALIAN, ORGANIZED, COLORECTAL CANCER SCREENING PROGRAM

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Introduction: Post-colonoscopy adverse events are a key quality indicator in population-based colorectal cancer screening programs, affecting safety and costs. Aim of this study was to assess colonoscopy-related adverse events and mortality in an organized screening setting.

Aims & Methods: In a cohort of patients undergoing colonoscopy within a screening program (Faecal Immunochemical Test every 2 years between 50 and 69 years or post-polypectomy surveillance) in Italy between 2002 and 2014, we retrieved patient, procedure and hospital related data to assess the rate of 30-day colonoscopy related adverse events and mortality. In detail, any unplanned admission within 30 days of a screening colonoscopy was reviewed blindly by two endoscopists to capture any possible adverse event. Death certificate registry were also matched with the endoscopy database. The association of each outcome with patient or procedure related variables was assessed with multivariate analysis.

Results: A total of 117,881 screening colonoscopies (66,584, 56.5%, with polypectomy) were included. Overall, 497/117,881 (0.42%) adverse events occurred, of which 281 (0.24%) bleeding and 65 (0.05%) perforations, corresponding to rates of 3.7‰ and 0.7‰ in operative and diagnostic procedures, respectively ($p<0.001$). At multivariable analysis, post-colonoscopy bleeding was associated to polyp size (≥ 20 mm: OR 16.29, 95%CI: 9.39-28.29), proximal location (OR 1.46, 95%CI: 1.14-1.87), and histology severity (high-risk adenoma, OR 5.6, 95%CI: 2.43-12.91), while post-colonoscopy perforation was associated to endoscopic resection (OR 2.91, 95%CI: 1.62-5.22), polyp size (OR 4.34, 95%CI: 1.46-12.92) and proximal location (OR 1.94, 95%CI: 1.12-3.37). Post-colonoscopy death occurred in 12/117,881 (0.001%) cases.

Conclusion: In an organised screening program, post-colonoscopy adverse events are a rare but not negligible eventuality. The most frequent is post-polypectomy bleeding, especially after resection of large (≥ 20 mm) and proximal lesion, indirectly supporting a policy of selective clipping.

Disclosure: Nothing to disclose

P1251

DIFFERENCES IN PATHOLOGICAL AND MORPHOLOGICAL FEATURES OF DEPRESSED-TYPE COLORECTAL NEOPLASMS

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Introduction: Colorectal cancers have two development theories. One is "adenoma-carcinoma sequence" theory. The other is considered to emerge directly from normal epithelium, not through the adenomatous stage. This theory is called "de novo" pathway. We aimed to investigate clinicopathological characteristics and long-term prognosis mainly on depressed-type colorectal carcinomas considered as "de novo" pathway.

Aims & Methods: A total of 37,134 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our center from April 2001 to December 2019. Of these, 1,330 lesions were T1 carcinomas. According to the developmental morphology classification, they were divided into 3 types: 292 lesions (22.0%) were depressed-type, 476 lesions (35.8%) were flat-type and 561 lesions (42.2%) were protruded-type. We analyzed the pathological difference of these lesions.

Results: The rate of distant metastasis or recurrence was 1% (10/1,330). Among these 10 cases, 5 cases were depressed-type lesions among which one showed a para-aortic lymph node metastasis and four showed a lung metastases.

Among T1 carcinomas, the rates of vessel invasion were 48% in depressed-type, 22% in flat-type and 21% in protruded-type, that of poorly differentiated or mucinous adenocarcinoma was 16%, 10% and 14%, that of massively submucosal invasion was 94.5%, 71.3% and 77.5%, and that of tumor budding was 34.5%, 14.8% and 16.9%, respectively. The rates of these pathological factors were significantly higher in depressed-type lesions than other types.

On the other hand, the rate of adenomatous component was 5.1%, 56.7% and 51.5%, and the rate of polypoid growth was 13.8%, 57.4% and 96.4% respectively. It was significantly lower in depressed-type lesions, suggesting that they emerge directly from normal epithelium without going through the adenomatous stage. The rates of lymph node metastasis were 8.7%, 3.1% and 10.2%, respectively, in which no significant difference was found in these three types.

Conclusion: Depressed-type colorectal neoplasms contained worth pathological features than other types. Giving a careful attention to the depressed neoplasms is important in the diagnosis and treatment of colorectal carcinomas.

Disclosure: Nothing to disclose

P1252 WITHDRAWN

P1253

FALSE POSITIVES IN FECAL IMMUNOCHEMICAL TEST IN COLORECTAL CANCER SCREENING AND THE RELATION WITH HARMFUL GASTROINTESTINAL DRUGS: THE IMPORTANCE OF THE EFFECT OF COMBINING PPI AND GASTROINTESTINAL DAMAGING DRUGS

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Introduction: False positive (FP) results in the fecal immunochemical test (FIT) as part of colorectal cancer screening constitute a clinical challenge. The intake of proton pump inhibitors (PPI) combined with antiplatelet agents (AA), anticoagulants (AC), selective serotonin reuptake inhibitors (SSRIs) or non-steroidal anti-inflammatory drugs (NSAIDs) could increase FP rate due to the inability of PPI therapy to protect gastrointestinal mucosa distal to the ligament of Treitz and its influence on the gut microbiome, which can increase the potential gastrointestinal damage of the PPI associated drugs.

Aims & Methods: The study aims to determine the influence of drug intake in the FP FIT results.

Prospective cohort study about patients undergoing a colonoscopy in the setting of colorectal cancer screening program due to positive results in FIT. True Positive (TP) was considered if tubular adenoma (TA), tubulovillous adenoma (TVA), villous adenoma (VA), sessile serrated adenoma (SSA), traditional serrated adenoma (TSA) or adenocarcinoma were found. Normal colonoscopy or the absent of any neoplastic or preneoplastic lesions such as hyperplastic polyps were considered as false positive (FP).

Age, sex, and drug intake (PPI, AA, AC, SSRIs, NSAIDs) data were collected for each patient. Logistic regression models were performed to evaluate if the intake of each drug alone or in combination were independent factors to FP FIT result.

Results: 515 patients were included with a mean age of 60±5; 59% (304/515) were males. The use of any drugs alone or in combination was observed in 50,5% (260/515) patients; 26,5% (69/260) of them used PPI alone, while 48,1% (125/260) took PPI combined with other potentially harmful gastrointestinal drugs. Finally, 25,4% (66/260) of patients consumed any of these drugs without PPI. There was a 48,3% (249/515) of FP FIT test in our cohort.

Drug intake was higher in > 60 years old group and female patients (p<0,001 and p=0,049 respectively). There were no statistically significant differences in PPI intake between males and females (p=0,354).

Multivariate logistic regression found as independent risk factor to FP test, female sex (OR=2,7 IC95%1,9-3,9), non-neoplastic colonic pathology (OR=1,5 IC95%1,1-2,2) and the use of any of the study drugs (OR=1,4 IC95% 0,9-2). Interestingly, in male subgroup analysis the risk of FP FIT

was significantly higher in PPI users (OR=1.8 IC95% 1,1-2,9) and when PPI use was combined with other drugs (combined intake Vs non-consumption: OR= 2 IC95%1,1-3,6).

Conclusion: Female, non-neoplastic pathology, and drug intake were identified as independent risk factors to FP FIT results. FP risk increased in males when PPI was combined with other gastrointestinal toxic drugs.

Disclosure: Nothing to disclose

P1254

ENDOSCOPIC FULL-THICKNESS RESECTION FOR THE MANAGEMENT OF DIFFICULT COLORECTAL LESIONS: A PROSPECTIVE COHORT STUDY

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Introduction: Endoscopic full-thickness resection with an over-the-scope device (FTRD system) is a useful tool for en-bloc and transmural resection of colorectal lesions unsuitable or difficult to remove both with standard and advanced endoscopic resection techniques.

Aims & Methods: The aim of this study is to evaluate the safety and efficacy of endoscopic full-thickness resection for the management of difficult colonic lesions.

Prospective cohort study of sequential patients referred to two tertiary referral centers for management of difficult colonic lesions. The procedures were performed by different endoscopists without previous experience with this device. We used descriptive analysis, Student's t-test, Wilcoxon sum rank test and Chi square tests as appropriate.

Results: We included 20 patients from two tertiary referral centers (70% male; median age 71.5 years, inter-quartile range [IQR] 65.5-80.0). About half of patient had cardiovascular comorbidities and 15% were receiving antiaggregants other than low-dose aspirin or anticoagulant therapy at the time of procedure. Indications for full-thickness resection included malignant histology or malignant appearing pit-pattern (40%), recurrence of lesions after previous endoscopic resection/surgery or non-lifting sign (50%), and intradiverticular or intrapendicular location (10%). The lesions were located at the rectum (25%), sigmoid (15%), descending colon (15%), ascending colon (20%), cecum (20%) and surgical anastomosis (5%). The lesions had a mean size of 19 mm (range 9-40 mm), and there was no significant difference in size between lesions located at the left or right colon (mean size 18 mm in the right colon and 19.5 mm in the left colon; p=0.70). The technical success of the full thickness procedure was 95% (in one case the procedure was not feasible because of difficult location), and lasted for a median 15 minutes (IQR 15-20).

Even though lesions located on the right colon were more difficult to reach, the overall procedural time was not significantly different between left and right colonic locations (mean 15 vs 18 min, respectively; p=0.20). There were no immediate peri-procedural complications. In three cases (16%) the procedure was done in the outpatient setting, while the remaining cases were done as inpatients. Of those who were hospitalized, all but one patient (94%) were discharged on the successive day.

There were no statistical significant differences in patient or procedural characteristics between those treated as inpatient or outpatients (p>0.05 in all cases). During a median follow-up of 5 months (IQR 0-17 months), there was one severe complication, consisting of acute appendicitis requiring surgery.

During follow-up we observed recurrences in two patients (17%), both small (< 10 mm) adenomatous recurrence about 6 months after the procedure, that were removed with biopsy forceps and/or argon plasma coagulation.

Conclusion: Endoscopic full-thickness resection is a safe and effective method of treating malignant or difficult colonic lesions. The procedure is not time-consuming and can be performed by expert endoscopists with minimal prior experience with the device. Larger prospective studies are needed to confirm these results.

Disclosure: Nothing to disclose

P1255

STRUCTURE-FROM-MOTION ANALYSIS MAY GENERATE AN ACCURATE AUTOMATED BOWEL PREPARATION SCORE

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Introduction: Inadequate bowel preparation is associated with missed lesions during colonoscopy. The quality of bowel preparation is usually scored by endoscopists using scales such as the Boston Bowel Preparation Score which are subject to inter-observer and intra-observer variability. Structure-from-Motion (SfM) is a computer vision technique which allows us to estimate the 3D structure of a scene from a set of 2D images [1]. Our aim was to use this approach to automatically and objectively assess the quality of bowel preparation.

Aims & Methods: We applied SfM to 15 colonoscopy sequences, composed of 150 to 300 consecutive images displaying different colon sections undergoing minimal biological deformations [2]. We then refined the estimated 3D meshes by smoothing them and eliminating erroneous estimates mainly arising at the edge of the reconstructed surfaces [3]. These erroneous estimates were generally due to a lack of visual redundancy, motion blur or illumination artefacts such as large specularities. Visual artefacts could be automatically detected and colon structure estimation and refinement could be combined in an efficient pipeline [4]. We however relied on a more robust and extensive SfM approach to generate dense surface reconstructions.

Results: We observed that SfM allows successful estimation of 3D structure of different colon sections. Reconstructing depressed and protruded areas could particularly facilitate visual analysis. Although SfM suffers from a scale ambiguity which prevents 3D measurements, it can provide different quality indicators such as an estimate of the percentage of colonic surface observed during a procedure. Unlike 2D quality indicators, 3D indicators are consistent and can be estimated over large colon sections. Here, we evaluated effectiveness of pre-operative bowel preparation by measuring the ratio of obscured or partially obscured area over the 3D surface reconstructed. For comparison purposes, we evaluated the proposed 3D indicator on 5 colonoscopy videos displaying caecum. Efficient and clean bowel preparation led to a percentage of obscured mucosa less than 2 %.

Conversely, poor bowel preparation corresponded to approximately 20% of the observed colon section obscured. For some images of the corresponding colonoscopy sequence, 35% of colon surface observed was obscured. This corresponded to 40% of the image pixels being obscured which illustrates the significant bias induced by 2D measurement. Such an

error would accumulate while assessing bowel preparation quality over large colon sections observed in multiple frames. Relying on quality indicator based on 3D estimations would contribute to an objective assessment of colonoscopy examination reliability.

Conclusion: This study demonstrates that 3D vision-based approaches can provide objective quality indicators in colonoscopy. More advanced approaches such as Simultaneous Localisation And Mapping (SLAM) could also be used to estimate both the 3D structure of the observed scene and the endoscope motion [4]. Combined with non-rigid SfM method, SLAM could provide practitioners with enhanced visualisation in colonoscopy. Artificial Intelligence approaches allowing the semantic interpretation of colonoscopy images would contribute to the development of advanced, robust and automated quality indicators.

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P1256

RAPID EXPANSION OF THE USE OF UNDERWATER MUCOSAL ENDOSCOPIC RESECTION OF COLONIC POLYPS

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Introduction: Injection-assisted conventional endoscopic mucosal resection (EMR) is established as a common method for resection of colonic sessile or flat polyps.

Randomized studies have shown that the "underwater" endoscopic technique decreases sedation needs, improves patient comfort and adenoma detection rate. At the same time, the underwater resection has been shown to increase the resection efficiency block of major lesions compared to conventional EMR.

Aims & Methods: During 15 months (10/2018-02/2020) we collected resection data endoscopic procedures performed in our Endoscopy Unit. Lesions larger than 15 mm in diameter, or smaller in size in locations of technical difficulty (appendicular, on a post-polypectomy scar, juxta-hemorrhoidal, juxta-diverticular and fibrotic retraction), have been selected.

Results: 107 resections were evaluated in 102 patients, with a mean age of 70 years, performed by 3 endoscopists, with experience in EMR, and less initial baggage in resection for underwater technique (UEMR). Most lesions were granular laterally spreading LST-G (37,9%), non-granular LST-NG (20,3%) and sessile (15%), localized mostly in the proximal colon (cecum 17,7%, ascending colon 16.8%), and in locations of difficult resection (post polypectomy scar 14%, appendix 7.4%, close hemorrhoids 3.7%, close diverticulum 2.8%.

45% of cases were removed by EMR (25,2% piece-meal and 19.6 in block), 54,2% with UEMR (32,7% in piece-meal and 21,5% in lock) Graphic 1. Two post-UEMR complications with delayed hemorrhage were detected at 7th and 14th day, while 7 patients with EMR presented an episode of early bleeding post polypectomy, and 4 patients had delayed bleeding during the next 14 days. No perforations had been documented. At this moment we've been done 35% of the control endoscopies (38/107), detecting residual lesion in 9 patients, completely removed.

EMR block	21	19,6%
EMR piece-meal	27	25,3%
UEMR block	23	21,5%
UEMR piece-meal	35	32,7%
ESD	0	0
TOTAL	107	100%

[Polypectomy technique]

Conclusion:

- The introduction in our unit of "underwater" endoscopic mucosal resection (UEMR), presents a learning curve relatively fast, with a very good safety profile, and has allowed us to remove larger block lesions or the treatment in areas of difficult submucosal elevation, rather than the conventional technique

- Awaiting post-resection control colonoscopies to assess the rate of a residual lesion, our partial data guide us to continue combining the two resection techniques according to the experience of professional, location and type of lesion.

Disclosure: Nothing to disclose

P1257

OUTCOMES OF ENDOSCOPIC MUCOSAL RESECTION FOR COMPLEX POLYPS: A DISTRICT GENERAL HOSPITAL EXPERIENCE

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Introduction: The SMSA (size, morphology, site, access) polyp scoring system is an established method of predicting critical outcomes of EMR (Endoscopic Mucosal Resection), specifically technical success, adverse events, and recurrence.¹

Aims & Methods: The aim of this study was to evaluate the efficacy of running parallel dedicated EMR lists between 3 senior endoscopists at a large district general hospital based on SMSA scores for difficult polyps. We retrospectively reviewed consecutive patients undergoing EMR of large (≥ 30 mm) colorectal polyps at The Royal Oldham Hospital, UK between 2015-2017. Electronic database was used to review endoscopic and histological data and to identify technical success, adverse events and follow up plans. A note was made on any recurrences and management up to 12 months after the initial EMR. SMSA score was calculated for each polyp and correlated with procedure related data.

Results: Seventy-four polyps were removed by EMR for 67 patients (40.3% females). Mean age was 74.5 years (Median 75, IQR 10) with 11 patients (16.9%) having ASA I, 39(60%) ASA II, 12(18.5%) ASA III and 1(1.5%) having ASA IV status. The mean size of the polyps was 49.3 mm (Median 45, IQR 25) with 48.6%(36) being flat, 33.8%(25) pedunculated and 16.6%(13)

sessile. Based on SMSA scores 43.2%(32) were level 3 and 56.8%(42) were level 4. Endoscopically incomplete resection was noted for 10.8%(8) with 12.5%(1) being level 3 and 87.5%(7) level 4 polyps. Based on histopathology tubulovillous adenoma was reported for 87.8%(65), adenocarcinoma 6.8%(5) and 1 case each for tubular, serrated, and villous adenoma and 1 hyperplastic polyp. Bleeding was noted as a complication in 6 procedures with 1 patient requiring blood transfusion and all 6 being SMSA level 4 polyps. There were no perforations noted. 2-6 month surveillance was performed following 32 procedures and recurrence was noted for 10 (2-level 3 & 8-level 4) with 9 requiring further EMR and 1 being referred for surgery. 12-14 months surveillance scope was performed following 28 procedures and recurrence was noted for 4 (2 each for level 3 & 4) with 3 undergoing further EMR and 1 being referred for surgery. No statistically significant difference was noted for recurrence at 2-6 months and 12-14 months follow up between level 3 and level 4 polyps (OR 0.19, p=0.139 & OR 0.85, p=0.877).

Conclusion: We achieved high success rates and low complications for complex polyps at a district general hospital. Having dedicated EMR lists running in parallel with 3 senior endoscopists helped achieve similar outcomes for SMSA level 3 and level 4 polyps. We highlight the importance of appropriate use of skills for running successful EMR lists at a district general hospital for complex polyps.

References: 1 Sidhu M. et al. 2018. Endoscopy, 50(07), pp.684-692.

Disclosure: Nothing to disclose

P1258

ASSESSMENT OF THE FECAL IMMUNOCHEMICAL TEST CUTOFF LEVEL IN SCREENING POPULATION DEPENDING ON GENDER

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Introduction: The quantitative fecal immunochemical test (FIT) is directly related to the risk of advanced lesions of colorectal cancer (CRC). Previous studies suggest that we might consider a different FIT cut-off based on gender, due to the different prevalence of CRC.

Aims & Methods: The primary aim of this study is to evaluate the relationship between gender, quantitative FIT level, and colonoscopy results to assess the need to change the cut-off level between men and women in CRC screening.

Patients referred for colonoscopy because of a positive FIT in the context of CRC screening program were prospectively included. The result ≥ 20 μ g Hb/g of feces (117 ng Hb/ml buffer) was considered a positive FIT. We collected the quantitative level of FIT, sex, and age of patients who were divided according to the colonoscopy findings into non-advanced pathology (NAP) (no polyps or non-advanced adenomas/serrated polyps) and advanced pathology (AP) (advanced adenomas/serrated polyps and CRC). A multivariate logistic regression analysis was used to estimate the risk of AP.

Results: 515 patients were included, with an average age of 60 ± 5 years; 59% (304/515) were men. AP was present in 37.1% (191/515) of patients, of which 12.6% were CRC (24/191). The median FIT level was 381 ng/ml (117-511900 ng/ml). There were statistically significant differences between the median FIT level in men (438.5 ng/ml, 117-511900 ng/ml) and women (324 ng/ml, 118-61500 ng/ml) (p = 0.007) and between NAP (313 ng/ml), 117-

61500 ng/ml) and AP (522 ng/ml, 118-511900 ng/ml) ($p < 0.001$). Among patients with AP, 72.3% (138/191) were male ($p < 0.001$). There were no statistically significant differences between the median FIT level and age over or under 60 years ($p = 0.362$). In the multivariate analysis, a higher risk of AP was found in when compared to women (OR = 2.3 CI95% 1.6-3.5). In the male group, the AP risk increases as the FIT quartiles increase (compared to first quartile: OR Q2 = 1.8 CI95% 1.3-2; OR Q3 = 2.5 CI95% 1.5-4.4; OR Q4 = 3 CI95% 1.7-5.3).

Furthermore, for the same FIT quartile men have a higher risk of AP than women, being significant from the second quartile onwards; i.e. OR Q4 in males versus women = 3.1 CI95% 1.4-7.1). In a secondary analysis, there were no statistically significant differences in the median FIT level between adenomas and serrated polyps ($p = 0.914$).

Conclusion: In our sample, male gender has a higher median FIT level, more frequent AP, and a higher risk of AP compared to women. This disparity in the diagnostic rate between sexes could be solved by increasing the cut-off level in women or decreasing that of men, two options to be chosen depending on the demand and supply of colonoscopies in each hospital service.

Disclosure: Nothing to disclose

P1259

DELAYED BLEEDING AFTER ENDOSCOPIC MUCOSAL RESECTION OF COLORECTAL LESIONS >20MM: EXTERNAL VALIDATION AND UTILITY OF THE GSEED-RE2 CLINICAL SCORE

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Introduction: Delayed bleeding after endoscopic mucosal resection (EMR) of colorectal lesions is a significant problem with an incidence of up to 10%. The GSEED-RE2 clinical score was recently proposed as a tool to assess patients at high risk of bleeding after EMR. Our purpose was to externally evaluate the usefulness of GSEED-RE2 in clinical practice.

Aims & Methods: Application of the GSEED-RE2 score to a prospective cohort of colorectal lesions >20mm submitted to endoscopic mucosal resection between 2009 and 2019 in a single unit. GSEED-RE2 parameters: use of antiplatelet / anticoagulants (3 points), proximal to hepatic flexure (3 points), size ≥ 40 mm (2 points), ASA ≥ 3 / comorbidities (1 point); High risk ≥ 7 . Delayed bleeding defined as presence of at least 2 of 3: (1) abundant haematochezia / dizziness; (2) drop in haemoglobin > 2 g/dL; (3) reduction in blood pressure > 20 mmHg or increase in heart rate $> 20\%$. Clip closure was an exclusion factor. Collection of demographic and clinical data, evaluation by logistic regression with Odds Ratio (OR) and determination of the area under the curve (AUC).

Results: Included 409 resected lesions in 382 patients, 58% males, median age 69 (IQR13). Lesions with a median size of 30mm (IQR15). Location proximal to hepatic flexure (43%), size ≥ 40 mm (34%), antiplatelet / anticoagulant (28%), ASA ≥ 3 / comorbidities (26%). Bleeding after EMR was registered in 18 cases (4.4%), although Delayed bleeding criteria only in 11 (2.7%). Stratification by risk group for delayed bleeding: High 14.8% (5/33); Intermediate 2.7% (4/148); Low 0.9% (2/228). Median score of 3 (IQR 3). Of the GSEED-RE2 parameters, only the use of antiplatelet / anticoagulants was statistically significant in our cohort (OR 7.3, 95% CI 1.9-28). Additionally, intra-procedural bleeding was also a risk factor (OR 11.7, 95% CI 1.1-128) while the use of prophylactic argon-plasma was a protec-

tive factor (OR 0.2, 95% CI 0.1-0.8). The application of GSEED-RE2 resulted in an AUC of 0.76 (95% CI 0.59-0.93), overlapping the original score cohort (AUC 0.74, 95% CI 0.67-0.80).

Conclusion: The use of the GSEED-RE2 score is externally validated. Its ability to predict delayed gastrointestinal bleeding after colon EMR is reasonable to good. Its application in clinical practice should be done with caution.

Disclosure: Nothing to disclose

P1260

DOES POLYP DETECTION RATE ACCURATELY REFLECT ADENOMA DETECTION RATE?

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Introduction: Thorough mucosal examination at colonoscopy is essential to detect pathology and ensure high quality procedures. Adenoma detection rate (ADR), defined as the number of colonoscopies where at least one adenoma is detected, is the most important marker of colonic mucosal visualisation and therefore of colonoscopy quality. Histology results are required, making the use of ADR challenging. Polyp detection rate (PDR) is more readily available as it can be collected directly from endoscopy reporting systems. The use of PDR as a substitute for ADR has been deemed acceptable providing it accurately reflects ADR (1).

Aims & Methods: We aim to investigate whether PDR can be used as a marker of colonoscopy quality. Data were collected from independent endoscopists in eight hospitals in England over a six-month period, including; ADR, PDR, PDR excluding rectal hyperplastic polyps (RHP), mean patient age. The ADR:PDR ratio (APDRQ) per endoscopist and Pearson correlation between ADR and PDR were computed, including and excluding rectal hyperplastic polyps. Multiple linear regression analysis was used to develop a model to predict an endoscopist's ADR from their PDR.

Results: 9265 colonoscopies performed by 118 endoscopists were included. Mean ADR and PDR per endoscopist were 17% (range 0-36.3, sd 7.37) and 27.2% (range 0-57.5, sd 9.3), respectively. The mean APDRQ was 0.60 (range 0-1.00, sd 0.21); this was 0.64 (range 0-1.17, sd 0.21) when RHPs were excluded. ADR and PDR were strongly correlated ($\rho = 0.75$, $p < 0.001$; $\rho = 0.80$, $p < 0.001$ after excluding RHP). Colonoscopists who scoped patients with mean age ≥ 60 years had higher mean ADRs (≥ 60 years: 17.4%, sd 7.4; < 60 years: 26.5%, sd 8.9). A similar pattern was seen for PDR (mean patient age < 60 years: 26.5%, sd 8.9; ≥ 60 years: 27.7%, sd 9.5). ADR was more accurately predicted by a combination of PDR and mean age of patients ($\text{ADR} = 0.54 * \text{PDR} + 0.26 * \text{mean patient age}$).

Conclusion: This study demonstrates that PDR can accurately be used as a marker of ADR as long as age is also considered.

References: 1. Rees CJ et al. UK key performance indicators and quality assurance standards for colonoscopy. Gut 2016;65:1923-9

Disclosure: Nothing to disclose. *L Neilson and R Dew are joint first authors

P1261

ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OFFERS A SAFER AND MORE COST EFFECTIVE ALTERNATIVE TO TRANSANAL ENDOSCOPIC MICROSURGERY (TEM): AN INTERNATIONAL COLLABORATIVE STUDY

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Introduction: Endoscopic submucosal dissection (ESD) and transanal endoscopic microsurgery (TEM) are minimally invasive procedures to treat early rectal cancer. Both are efficacious, yet there are few studies comparing the techniques. The aim of our study was to compare the safety and efficacy of ESD versus TEM for treatment of early rectal cancer.

Aims & Methods: Between January 2016 and November 2019, patients with early rectal cancers who were managed with either ESD or TEM at seven academic centers internationally were included. Data were gathered retrospectively and analyzed with respect to clinical success, technical success, tumor type, tumor size, procedure time, adverse events, recurrence rates and length of hospital stay.

Results: A total of 204 patients were included: ESD (n=101) or TEM (n=103). Age and BMI were not statistically different between the two groups. Mean tumor size was 42.2mm +/- 23.9 in the ESD group and 70.4mm +/- 27.9 in the TEM group, significantly larger in the latter (p < 0.00001). Average procedure time was 131.5 +/- 67.9 minutes in the ESD group and 104.9 +/- 28.4 minutes in the TEM group (p=0.000347). Average length of hospital stay was 3.3 +/- 2.6 days in the ESD group and 4.7 +/- 0.7 days in the TEM group (p< 0.00001). The rate of adverse events was 6.8% in the ESD group and 24% in the TEM group. There was no significant difference in the rate of en bloc resection, technical success, tumor location, necessity of additional procedures and tumor recurrence rates.

Conclusion: As compared to TEM, ESD is a safer procedure with shorter hospital stays and should be offered for patients who have early rectal tumors. This is presently the largest study comparing the two treatment modalities. A prospective randomized control trial is now warranted.

Disclosure: Nothing to disclose

P1262

A VALIDATED PATIENT REPORTED EXPERIENCE MEASURE FOR GASTROINTESTINAL ENDOSCOPY: THE NEWCASTLE ENDOPREM™

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Introduction: Gastrointestinal (GI) endoscopy and computed tomography colonography (CTC) are crucial diagnostic and therapeutic procedures. Measuring patient experience of GI procedures allows evaluation of quality of patient care, identification of areas requiring improvement and, hence, helps optimise patient outcomes.¹ Patient Reported Experience Measures (PREMs) should be patient-derived, however current measures are clinician derived.²

Aims & Methods: This study used the patient's perspective to develop a PREM for GI procedures. The study comprised four phases. Phase 1: -qualitative semi-structured interviews with patients who had recently undergone endoscopy/CTC. Thematic analysis identified important aspects of experience, and determined whether these were similar, or differed, across GI modalities. Phase 2: A draft PREM was developed from the phase 1 analysis and refined by the study team. Further refinement was undertaken in rounds of cognitive interviews with patients. Phase 3: The pilot PREM was prospectively administered, for self-completion, to patients following a GI procedure at four sites in North East England. The psychometric properties of the PREM were investigated. Phase 4: Review and revision.

Results: Phase 1: Six themes were identified from 35 patient interviews: anxiety, expectations, information & communication, embarrassment & dignity, choice & control and comfort. These were seen for colonoscopy, OGD and CTC. Phase 2: Themes were structured by procedural stage (before the procedure, at the hospital, during the procedure, after the procedure). The draft PREM was refined iteratively during five rounds of cognitive interviews with 15 patients. Phase 3: Between October 2017 and September 2018 the pilot PREM was prospectively administered, for self-completion, to 1650 patients. The response rate was 48.4% (n=799). The instrument had good psychometric properties and was found to contain 7 subscales. Phase 4: Redundant questions were removed, some wording was refined, and the questionnaire finalised. The final instrument includes 54 questions.

Conclusion: The Newcastle ENDOPREM™ assesses all aspects of the GI procedure experience. It will be used for measuring patient experience in clinical practice and within endoscopy trials. The PREM is now undergoing international validation.

References: 1. Rees CJ et al. BSG position statement on patient experience of GI endoscopy. Gut 2019; DOI: 10.1136/gutjnl-2019-319027 2. Brown S et al. Patient-derived measures of GI endoscopy: a meta-narrative review of the literature. Gastrointest Endosc 2015;81(5):1130-40

Disclosure: Nothing to disclose

P1263

MEASURING PATIENT EXPERIENCE OF GI ENDOSCOPY: PSYCHOMETRIC PROPERTIES OF THE NEWCASTLE ENDOPREM™

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Introduction: Gastrointestinal (GI) endoscopy and computed tomography colonoscopy (CTC) are widely performed investigations of the GI tract. Patient experience affects future uptake, attendance for surveillance and correlates with outcomes.¹ Current measures of experience are clinician and nurse-derived.² The Newcastle ENDOPREM™ was developed using a rigorous systematic process based on qualitative patient interviews.³

Aims & Methods: This study aimed to investigate the psychometric properties of the instrument. Patients aged ≥18 years, undergoing oesophagogastroduodenoscopy (OGD), colonoscopy or CTC at 4 sites in North East England were prospectively asked to complete the PREM. Using IBM®SPSS® 24, we examined response rates and patterns, missing values, floor and ceiling effects and item-total correlations. Exploratory factor analysis (EFA) was conducted using principal components analysis. Reliability of factors was assessed using Cronbach's α.

Results: 799 questionnaires were returned from Oct 2017 - Sept 2018 (response rate 48.4%). Respondents were aged 18-95 years (mean 65.3, SD 12.6), 43.3% were male and 41.1% had undergone OGD, 43.3% colonoscopy and 14.4% CTC. 24 of the 59 questions had a ceiling effect (>40% choosing the 'best' response). No questions had floor effects. For 3 questions, more than 5% of respondents failed to answer. The highest was 8.6%. The mean number of questions missed was 1.2; this was higher in older patients. 8 questions correlated poorly with others (rho<0.3) and were excluded from EFA. EFA showed 7 factors, explaining 61.5% of the variance. All factors had Cronbach's α >0.6, indicating good reliability.³

Conclusion: The Newcastle ENDOPREM™ has good psychometric properties. This analysis has enabled refinement of some questions and item reduction, resulting in a PREM, derived from patients' reports, which comprehensively assesses patient experience across GI investigative modalities.

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Disclosure: L Sharp and CJ Rees are joint senior authors

P1264

LOW COLONOSCOPY NUMBERS CORRELATE WITH POOR QUALITY COLONOSCOPY: RESULTS OF A REGIONAL STUDY

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Introduction: UK key performance indicators (KPI) and quality assurance standards for colonoscopy have been established in order to ensure minimal standards and reduce unacceptable variation in quality.[1] Included within these standards is the requirement for a minimum of 200 colonoscopies to achieve competence and 100 per annum to maintain competence. We investigated the link between number of procedures and the minimal standards for two other KPIs- caecal intubation rate (CIR) and adenoma detection rate (ADR).

Aims & Methods: Data were collected from 118 endoscopists in eight hospitals over a six-month period. Gastroenterologists, surgeons and nurse endoscopists were included. The link between three KPIs was investigated; ≥100 colonoscopies in 12 months (as six-month data was collected, ≥50 procedures in this timeframe were used); CIR ≥90% and ADR ≥15%. Associations between pairs of KPIs were tested. Multiple logistic regression was used to investigate inter-relationships between KPIs and additional factors (including endoscopist grade, mean patient age, patient sex, hyoscine butylbromide use), with low ADR as the outcome variable.

Results: 118 endoscopists undertook 9,265 colonoscopies in six months. The mean number of colonoscopies conducted in six months was 78.5 (range 4-334, standard deviation (sd) 61). The mean ADR and CIR were 17% (range 0-36.6, sd 7.37) and 91.2% (range 55.5-100, sd 6.6), respectively. 61% of endoscopists achieved ADR ≥15%, 65% had CIR ≥90% and 64% performed ≥50 colonoscopies in six months. Of those who performed ≥50 colonoscopies in six months, 68% met ADR and 69% CIR performance metrics. 29% of colonoscopists met all three KPIs.

36% of colonoscopists performed < 50 colonoscopies in six months (mean 27.6 procedures, sd 12.5). In this group, mean ADR was 13.2% (sd 8.1) and mean CIR was 89% (sd 9.6). 49% had ADR ≥15% and 58% had CIR ≥90%. 33% met both KPIs for ADR and CIR.

Total number of colonoscopies and ADR were significantly associated (p=0.04), but total colonoscopies and CIR were not. In multiple regression analyses, undertaking fewer colonoscopies and using hyoscine butylbromide less frequently was significantly associated with ADR < 15. CIR, endoscopist grade, % male patients, mean patient age and CIR were not significantly related to ADR < 15.

Conclusion: Colonoscopists who perform less than the nationally stipulated minimum of 100 procedures per year have significantly lower ADRs. National guidance should be followed with all colonoscopists performing > 100 procedures per year.

References: 1. Rees CJ et al. UK key performance indicators and quality assurance standards for colonoscopy. *Gut* 2016;65:1923-9

Disclosure: LJ Neilson and R Dew are joint first authors

P1265

A RANDOMIZED PROSPECTIVE STUDY EVALUATING EFFECTIVENESS OF A DOUBLE BALLOON ENDOLUMENAL PLATFORM FOR COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic removal of colorectal polyps and early cancers eliminates the need for surgical resection and the potential of a temporary or permanent colostomy. This less invasive approach decreases treatment cost, morbidity/mortality, and assures an earlier return to regular physical activity. Endoscopic mucosal resection (EMR) of colonic lesions over 2 cm in size requires piecemeal resection with significant rates of post-procedural recurrence.

Endoscopic submucosal dissection (ESD) allows *en bloc* removal of colonic lesions, hence drastically reducing post-procedural recurrence. However, ESD remains technically difficult, time-consuming, and a labor-intensive procedure performed in a limited number of specialized high-volume centers. A double balloon endolumenal platform (DBEP) is comprised of a flexible sheath preloaded over any colonoscope with two expandable balloons; one balloon is firmly attached to the proximal end of the device near the scope tip and another balloon which can be advanced and retracted by push-rods at the device base. The balloons and sheath assist advancement of the endoscope (and an endoscopic suturing device) through the colon, providing multi-directional dynamic retraction and improved scope stability during colonic EMR and ESD.

Aims & Methods: The study aim was to evaluate safety and time savings (cost-effectiveness) of colonic ESD assisted by a DBEP compared to traditional ESD. A prospective randomized (1:1) study was approved by IRB for removal of colorectal polyps ≥ 2 cm in size. The primary endpoint was ESD time in study (ESD with DBEP) and control (traditional ESD) groups. Secondary endpoint comparators included total procedure time (various time-points) and adverse events between the groups. Complications and safety were assessed during the procedure and through the 3-month follow-up visit. Enrollment was set at 200 total patients, assuming a 20-minute time savings with the test device. An independent study monitor reviewed and oversaw monitored data collection for quality assurance.

An interim analysis was scheduled after 140 intent to treat patients were enrolled to assess if recruitment could be closed due to the primary endpoint being met.

Results: Enrollment began in February 2019. Interim analysis was performed in February 2020. Study (N= 71) and control (N=69) groups were similar in lesion size (10.85 ± 11.38 vs 9.81 ± 12.40 cm²), age (66.0 ± 8.73 vs 65.8 ± 9.23) and gender (females 47.9% vs 53.6%). *En bloc* resection was achieved in 97.2% of the device group vs 87.0% of control group ($p=.03$). Use of the DBEP increased ESD speed over controls by 47.5% (14.52 ± 7.7 vs 7.62 ± 7.69 cm²/hour, $p<0.001$), shortened ESD time by 46.5% (47.21 ± 42.59 vs 88.28 ± 76.07 min, $p<0.001$) and decreased total procedure time by 37.7% (86.91 ± 41.43 vs 139.5 ± 83.19 min, $p<0.001$). There were no device related adverse events.

Conclusion: The double balloon endolumenal platform markedly facilitated colonic ESD and improved the rate of *en bloc* resection, dramatically increased dissection speed and significantly reduced dissection and total procedure time.

Disclosure: Dr. Kantsevov is consultant for Endocages, LumenDi, Medrobotics, Medtronic, Olympus, Slater Endoscopy, Vizballoons. Dr. Kantsevov is member of Advisory Board and holds equity in Endocages, Lumendi, Slater Endoscopy, Vizballoons.

P1266

NEW ENDOLUMENAL THERAPEUTIC PLATFORM: RESULTS OF THE FIRST 519 COLONIC INTERVENTIONS

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Introduction: Endoscopic submucosal dissection (ESD) allows *en bloc* removal of colon polyps and early colon cancer. Multiple studies demonstrated advantages of ESD over piecemeal endoscopic mucosal resection (EMR). However, ESD is technically difficult, labor-intensive and time-consuming procedure. A double balloon endolumenal platform was created to facilitate colonic EMR and ESD. The device is comprised of a flexible sheath preloaded over any colonoscope with two expandable balloons; one balloon is firmly attached to the proximal end of the device near the scope tip and another balloon which can be advanced and retracted by push-rods at the device base. The balloons and sheath assist advancement of the endoscope (and an endoscopic suturing device) through the colon, providing multi-directional dynamic retraction and improved scope stability during colonic EMR and ESD.

Aims & Methods: Study aim was to evaluate safety and effectiveness of new endolumenal double balloon platform for colonic ESD and EMR in a single center retrospective observational study. Colonoscope was preloaded with a double balloon platform and inserted into the colon till the colonic lesion was reached. After- (distal) balloon was inflated stabilizing position of the colonoscope and creating a conduit between the rectum and "therapeutic zone." Circumferential incision was performed using ESD knives. Then the dissected mucosal margin was clipped to a suture-loop attached to the fore- (proximal) balloon to provide multi-directional dynamic retraction facilitating submucosal dissection. After completion of the ESD colonoscope was removed and endoscopic suturing device mounted on a double-channel upper endoscope was advanced through the platform into the therapeutic zone. Complete suturing closure of the large mucosal defect post ESD was performed. Endoscope and therapeutic platform were removed and the patient was discharged home from endoscopy unit post procedure. Patients' demographic information, lesions' characteristics, procedural times and follow up data were retrospectively collected into Excel database and analyzed.

Results: From November 2017 till November 2019 new therapeutic endolumenal platform was used in consecutive 519 patients. Mean patient's age was 66.3 ± 10.6 years, 243 patients (46.8%) were females. Mean lesion's size was 3.6 ± 1.9 cm and 134 lesions (25.8%) were over 5 cm in size. Majority of the lesions were located in the cecum (152, 29.3%), ascending (180, 34.7%) and transverse colon (124, 23.9%). Delivery of the colonoscope loaded with therapeutic platform was technically easy and required only 11.9 ± 11.9 minutes to reach colonic lesion. ESD was performed in 454 patients (87.5%) with *en bloc* resection rate of 94.7% (430 patients). Stabilization of colonoscope with after-balloon and traction with suture-loops attached to the fore-balloon significantly facilitated colonic ESD, decreasing intervention time to 43.9 ± 44.8 minutes and total procedure time to 91.5 ± 90.1 minutes. Serving as a conduit, the platform allowed quick delivery of endoscopic suturing device from rectum to therapeutic zone in 2.3 ± 2.7 minutes.

Conclusion: New double balloon therapeutic platform markedly facilitates colonic ESD, decreases intervention time, total procedure time and serves as a conduit expediting delivery of the endoscopic suturing device into the right colon.

Disclosure: Dr. Kantsevov is consultant for Endocages, LumenDi, Medrobotics, Medtronic, Olympus, Slater Endoscopy, Vizballoons. Dr. Kantsevov is a member of Advisory Board and holds equity in Endocages, Lumendi, Slater Endoscopy, Vizballoons.

P1267 WITHDRAWN

P1268

DIFFERENTIAL DIAGNOSIS OF COLORECTAL LOW-GRADE ADENOMA USING ENDOCYTOSCOPY: A NOVEL POSSIBILITY FOR THE “RESECT AND DISCARD” STRATEGY

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Introduction: Recent opinions have expressed that if an endoscopic diagnosis of adenomas can be made with high accuracy, then, the omission of a pathological diagnosis following endoscopic resection is acceptable. Endocytoscopy (EC), a next-generation endoscopic system, facilitates observation at a maximum magnification of ×520. EC-based grading of dysplasia can be clinically effective for diagnosing adenomas, if such a diagnosis of adenomas, particularly of low-grade adenomas, can be made with high accuracy. To our knowledge, no study has reported high-precision diagnosis of colorectal low-grade adenoma, endoscopically. We aimed to reveal which endocytoscopic findings may be used as indicators of low-grade adenoma, and to assess whether a “resect and discard” strategy using endocytoscopy is feasible.

Aims & Methods: We retrospectively examined 748 lesions among the neoplastic lesions that could be observed by EC between May 2005 and July 2017. A normal pit-like structure in endocytoscopic images was considered a normal pit (NP) sign positive and used as an indicator of low-grade adenoma. The primary outcome was the diagnostic accuracy of the NP sign for low-grade adenoma. We evaluated agreement rates between endocytoscopy and pathological diagnosis for surveillance colonoscopy interval recommendation (SCIR) and performed a validation study to verify the agreement rates.

Results: A total of 497 lesions were classified as EC2 NP sign positive. Of these, low-grade adenomas accounted for 450 lesions and advanced lesions (high-grade dysplasia, tubulovillous adenoma, invasive cancer) accounted for 16. NP sign positive as an indicator of low-grade adenomas had a sensitivity of 85.0%, specificity of 90.7%, positive predictive value of 96.6%, negative predictive value of 66.1%, accuracy of 86.4%, and positive likelihood ratio of 9.2. The agreement rate between endocytoscopy and pathological diagnosis for SCIR was 94.3% (95% confidence interval [CI], 92.2%-96.1%; $P < 0.001$) under United States guidelines and 96.3% (95% CI, 94.5%-97.7%; $P < 0.001$) under European Union guidelines. All inter- and intraobserver agreement rates for expert and nonexpert endoscopists had k -values ≥ 0.8 except one nonexpert pair.

Conclusion: Endocytoscopy is a very effective modality in determining the differential diagnosis of colorectal low-grade adenoma and shows promise for future implementation with the “resect and discard” strategy.

Disclosure: Nothing to disclose

P1269

TREATMENT POLICY FOR COLONIC LATERALLY SPREADING TUMORS BASED ON EACH CLINICOPATHOLOGICAL FEATURE OF FOUR SUBTYPES: ACTUAL STATUS OF PSEUDO-DEPRESSED TYPE

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Introduction: Laterally spreading tumors (LSTs) are originally classified into four subtypes. Pseudo-depressed nongranular types (LSTs-NG-PD) are gaining attention because of their high malignancy potential. Previous studies discussed the classification of nongranular (LST-NG) and granular types (LST-G); however, the actual condition or indication for endoscopic treatment of LSTs-NG-PD remains unclear.

Aims & Methods: A total of 22,987 colonic neoplasms including 2822 LSTs were resected endoscopically or surgically at Showa University Northern Yokohama Hospital. In these LSTs, 322 (11.4%) were submucosal invasive carcinomas. We retrospectively evaluated the clinicopathological features of LSTs divided into four subtypes. In 267 LSTs resected en bloc, their submucosal invasion site was further evaluated. we aimed to compare the submucosal invasion pattern of LSTs-NG-PD with the other three subtypes.

Results: The submucosal invasive carcinoma rates were 0.8% in the granular homogenous type (LSTs-G-H), 15.2% in the granular nodular mixed type (LSTs-G-M), 8.0% in the nongranular flat elevated type (LSTs-NG-F), and 42.5% in the nongranular pseudo-depressed type (LSTs-NG-PD). Tumor size was associated with submucosal invasion rate in LSTs-NG-F and LSTs-NG-PD ($p < 0.001$). The multifocal invasion rate of LSTs-NG-PD (46.9%) was significantly higher than that of LST-G-M (7.9%) or LST-NG-F (11.8%). In LSTs-NG-PD, the invasion was significantly deeper ($\geq 1000 \mu\text{m}$) if it was observed in one site.

Conclusion: For LSTs-G-M and LSTs-NG-F that may have invaded the submucosa, en bloc resection could be considered. Considering that LSTs-NG-PD had a higher submucosal invasion rate, more multifocal invasive nature, and deeper invasion tendency, regardless if invasion was only observed in one site, than LSTs-NG-F, we should endoscopically distinguish LSTs-NG-PD from LSTs-NG-F and strictly adopt en bloc resection by endoscopic submucosal dissection or surgery for LSTs-NG-PD. This content has been accepted for publication in GASTROINTESTINAL ENDOSCOPY.

Disclosure: Nothing to disclose

P1270

COMPUTER AIDED CHARACTERISATION OF COLORECTAL POLYPS USING ARTIFICIAL INTELLIGENCE

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Introduction: Optical diagnosis is the in-vivo prediction of colorectal polyp histopathology. The ability to replace post-polypectomy histopathology assessment with optical diagnosis has significant economic benefits but inter-observer variability amongst endoscopists, particularly in non-academic centres, has limited its application in clinical practice. Artificial Intelligence (AI) using deep learning may lead to a new generation of clinical support tools capable of computer aided characterisation or diagnosis of polyps. Research in this field has often relied upon high quality still images or videos from expert endoscopists to train and test convolutional neural networks (CNN) resulting in selection bias.

Aims & Methods: An AI system was developed to optically characterise colorectal polyps using data collected prospectively from routine clinical practice. Data was collected from unaltered colonoscopy videos from 8 endoscopists at a single centre using Olympus 260 and 290 series scopes. Histopathological classification was recorded for each polyp.

The dataset was created using Narrow Band Imaging (NBI) and NBI-Near Focus (NBI-NF) video sequences, including images captured of polyps during the colonoscopy. Both imaging modalities were used to increase the generalisability of the CNN. Low resolution frames were excluded with the remaining frames annotated with bounding boxes around polyps and labelled with the histopathology. The annotations were referenced as the gold standard.

A ResNet-101 CNN pre-trained on ImageNet was developed to classify the visual appearance of colorectal polyps as adenomatous or non-adenomatous. During inference, the probability scores computed by the CNN were used as confidence for its prediction with a higher score reflecting increased classification confidence. 70% and above was defined as a confident polyp characterisation (adenomatous or non-adenomatous), less than 70% was deemed unclassified.

Results: The final dataset consisted of 187 confirmed polyps (122 adenomas, 48 sessile serrated lesions (SSL), 17 hyperplastic) from 71 patients with a total of 41,171 video frames. Data was split, as shown in table 1, into a training (~65%), validation (~5%) and testing set (~30%) with no overlap of data or patients. The testing set consisted of 64 polyps (41 adenoma, 16 SSL, 7 hyperplastic) from 26 patients, with a total of 11,821 frames.

The CNN achieved a confident diagnosis in 84% of frames in the test set. On a per-frame analysis, the accuracy of the CNN optical characterisation was 92%, with a sensitivity of 92% to diagnose adenomas and a specificity of 90%. In the receiver operating characteristic (ROC) analysis, the CNN achieved an area under curve (AUC) of 94%. On a per polyp analysis, the accuracy of the CNN characterisation was 91%, with a sensitivity of 93% to diagnose adenomas and a specificity of 87%.

Conclusion: A CNN was developed using prospective data from routine clinical practice. This has achieved promising results to differentiate adenomatous from non-adenomatous polyps. The CNN will undergo further training followed by assessment in a multi-centre randomised controlled trial.

	Training Dataset	Validation Dataset	Testing Dataset
Number of patients	38	7	26
Number of adenomas polyp (frames)	75 (22007)	6 (1143)	41 (8218)
Number of non-adenomatous polyps (frames)	40 (5412)	2 (788)	23 (3603)
Total number of frames	27419	1931	11821

[Table 1: Breakdown of the number of patients, polyps and frames per dataset]

Disclosure: Laurence Lovat - Minority shareholder in Odin Vision
Stoyanov - Minority shareholder in Odin Vision

P1271

COMPUTER-AIDED DETECTION OF COLORECTAL POLYPS USING A NEWLY GENERATED DEEP CONVOLUTIONAL NEURAL NETWORK

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Introduction: The use of artificial intelligence represents an objective approach to increase endoscopist's adenoma detection rate (ADR) and limit inter-operator variability. In this study, we evaluated a newly developed deep convolutional neural network (DCNN) for automated detection of colorectal polyps ex-vivo as well as in a first in-human trial.

Aims & Methods: For training of the DCNN 116,529 colonoscopy images from 278 patients with 788 different polyps were collected. A subset of 10,467 images containing 504 different polyps were manually annotated and treated as the gold standard. An independent set of 45 videos was used for ex-vivo performance testing. In vivo real-time detection of colorectal polyps during routine colonoscopy by the DCNN was tested in 36 patients in a back-to-back approach.

Results: When analyzing the test set of 15,534 single frames, the DCNN's sensitivity and specificity for polyp detection and localization within the frame was 90% and 80%, respectively, with an AUC of 0.92. In vivo, baseline PDR and ADR were 36% and 25% and increased to 50% and 33%, respectively, with the use of the DCNN. Sensitivity of the DCNN for polyp detection was 100%. Of the 11 additionally with the DCNN detected lesions, the majority were diminutive and flat, among them 3 SSAs. In 18 patients, at least one false positive detection occurred with a mean of 3 false positive hits per patient.

Conclusion: This newly developed DCNN enables highly sensitive automated detection of colorectal polyps both ex vivo and during first in-human clinical testing and could potentially increase the detection of colorectal polyps during colonoscopy.

Disclosure: Nothing to disclose

P1272

PRELIMINARY RESULTS OF THE OBESITY RELATED COLORECTAL ADENOMA RISK (OSCAR) STUDY

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Introduction: Obesity and non-alcoholic fatty liver disease (NAFLD) is associated with colorectal neoplasia.^{1,2} In the UK, colonoscopy is performed for patient symptoms, Bowel Cancer Screening Programme (BCSP), family history or surveillance. We aimed to further explore obesity and NAFLD as risk factors with a view to developing a risk model.

Aims & Methods: OSCAR was a cross sectional study recruiting patients attending for colonoscopy. Patients' medical history, smoking habits, alcohol intake, medication, family history of CRC, waist circumference/height/weight and bloods results were recorded. Multivariate logistic regression was undertaken to test associations between obesity, NAFLD, other risk factors and colorectal adenomas. Preliminary results are reported.

Results: 1430 patients were recruited (BCSP 410 [28.6%]; symptomatic 1020 [71.3%]). 698 were male (48.8%) with median age: 59 years. The burden of obesity and liver disease was high (reported in a further abstract). 457 patients (31.9%) had colorectal adenomas, 170 (11.9%) had advanced adenomas, and 59 (4.1%) had CRC.

Statin use, smoking, metabolic syndrome, abnormal fatty liver index and ALT level were significantly associated with adenoma in univariate analysis, but not in the multivariable model. Variables in the final multivariate model are displayed below. Neither obesity nor NAFLD (established diagnosis; patient reported or in medical notes) were independently associated with adenoma risk in univariate or multivariate analysis (Obesity: multivariable (mv) OR 1.14 [95%CI 0.9-1.4]; NAFLD: mvOR 0.7 [95%CI 0.3-1.5]).

Conclusion: Older age, referral route, alcohol excess and hypertension were significantly associated with colorectal adenoma. After accounting for these factors, obesity and NAFLD were not independently associated with adenoma. Further work is exploring adenoma burden and more detailed modelling.

Risk factor	mvOR	95%CI
Age		
• <60	1	-
• 60-74	1.51	1.10-2.06
• >74	2.29	1.36-3.85
Sex (Female as reference group, male as comparator group)	1.31	0.99-1.71
Referral route (Screening as reference group, symptomatic as comparator group)	0.22	0.16-0.29
Alcohol excess	2.05	1.26-3.33
Type II Diabetes	1.47	0.99-2.19
Hypertension	1.50	1.11-2.03

[Multivariable analysis for colorectal adenoma]

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Disclosure: Nothing to disclose

P1273

ENDOSCOPIC PROCEDURE AND ENDOSCOPISTS CHARACTERISTICS ASSOCIATED WITH THE DETECTION OF COLORECTAL LESIONS

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Introduction: Colonoscopy key performance measures have been described over the years to achieve high quality colonoscopies, and different factors may influence those performance measures from two sides: factors related to the procedure and factors related to the physician who performs the examination.

Aims & Methods: This multicenter and cross-sectional study across 13 centers aimed to analyze the influence of factors directly related to endoscopic procedure and endoscopists characteristics in the detection of colorectal lesions (adenomas and serrated polyps), and to analyze this influence according to the indication. Adults aged 40 to 80 years old, either outpatients or hospitalized, who underwent a colonoscopy at these centers between February 2016 and December 2017 were recruited using consecutive sampling. Endoscopists performing ≥50 examinations in our study were selected to evaluate the quality of physicians. Binary logistic regression analysis was used in the multivariate analysis for categorical variables (adenoma, advanced adenoma and serrated polyp detection rate (ADR, AADR and SDR, respectively)) and generalized linear model was used for quantitative data (adenoma and serrated polyp per colonoscopy rate (APCR and SPCR, respectively)).

Results: A total of 12,932 procedures in the same number of patients were included; 51.8% were men and the largest fraction of individuals were aged 50 to 69 years old (68.2%). Most of the endoscopic procedure indications were gastrointestinal symptoms (39.4%) and +FIT (37.2%), followed by post-polypectomy surveillance (15.2%) and primary screening

colonoscopies (8.2%). Adequate colon cleansing was obtained in 86.6% of patients and cecal intubation in 95.4%. Median withdrawal time was 8 min (25thP 6 - 75thP 10).

Of the 96 physicians included, 43.8% were women and the mean age was 41.9 years (SD±9.8). All of them were gastroenterologists from a tertiary hospital. Life-long number of colonoscopies performed ranged from 800 to 40,000 and the annual colonoscopy volume from 100 to 2,900; the mean hours per week dedicated to endoscopy was 23.8 hours (SD ± 12.4). 90% of endoscopists had assisted endoscopic educational activities in the previous 2 years.

Regarding quality indicators, the mean ADR, AADR and SDR of the 96 endoscopists participating in the study were 39.7%, 17.7% and 12.8%, respectively. There was a wide variation across physicians, that ranged from 13.2% to 74.0% with respect to ADR and from 3.3% to 27.4 regarding SDR. APCR was 0.97 and SPCR 0.22. In the multivariate analysis, withdrawal time resulted the only factor related with the detection of adenomas and serrated polyps in general (ADR OR 1.39 (1.34-1.43); AADR OR 1.36 (1.30-1.41); SDR OR 1.17 (1.13-1.22)) and when stratified by indication. Endoscopists factors influenced the detection of advanced adenomas (male OR 1.26 (1.11-1.43), age 0.98 (0.97-0.99)) and serrated polyps (age 0.99 (0.98-0.99)) with no impact in ADR. Differences between indications were detected, with more influence of physician characteristics in FIT+ procedures.

Conclusion: Withdrawal time is the most important factor related to the detection of colorectal lesions. Endoscopists characteristics influence advanced adenomas and serrated polyps. Additional procedure and physician factors variate according to the indication with specially in FIT+ procedures.

Disclosure: Nothing to disclose

P1274

EVALUATION OF COLORECTAL POLYPECTOMY PRACTICES IN PORTUGAL - A NATIONWIDE SURVEY FROM A WESTERN EUROPE COUNTRY

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Introduction: Colorectal cancer is one of the most common malignancies worldwide. Colonoscopy allows identification and removal of premalignant polyps. However, there are multiple polypectomy techniques available and significant variations of their use.

Aims & Methods: With this study, we aimed to assess the current polypectomy practice patterns among Portuguese endoscopists and verify if they followed the European guidelines for colorectal polypectomy. A 25-question electronic survey was created based on the standards set by the European Society of Gastrointestinal Endoscopy (ESGE) guideline for colorectal polypectomy. The electronic survey was sent to all members of Portuguese Society of Gastroenterology (SPG). Data were collected and managed using REDCap electronic data capture tools hosted at SPG - CEREGA.

Results: A total of 151 members completed the questionnaire, 52% female, with a median age of 34 years old [IQR 31-45].

Most respondents were consultants (69.5%), with 47.3% from tertiary hospitals vs 45% from regional hospitals, and 88.7% performed at least 10 colonoscopies per week (45.7% more than 20 per week).

Concerning right colon polypectomy, for polyps ≤3 mm cold biopsy forceps (CBF) was the most used (63.6%), while for 4-5mm and 6-9mm polyps cold snare polypectomy (CSP) was preferred (88.7% and 74.8%, respectively); in polyps ≥10mm, hot snare polypectomy (HSP) was the most chosen (58.9%). In left colon polypectomy, CBF was the most used for polyps ≤3 mm (60.9%) and CSP was the predominant choice for polyps 4-5mm and 6-9mm (90% and 76%, respectively); for polyps ≥10mm, HSP was preferred (72.2%). Endoscopic mucosal resection (EMR) was also an option for polyps ≥10mm, specially in the right colon (37.7% vs 23.8% in the left colon).

CSP was performed by 98.7%, but only 54.7% adjusted the technique (cutting the polyp without luminal traction) and only 40.9% used dedicated snares. Bleeding prophylaxis measures for high-risk pedunculated polyps were taken by 84.8%, mostly adrenaline injection (73.5%) and/or application of clips (52.3%).

Conclusion: CSP is underused for resection of polyps ≤ 3 mm, despite its known safety and efficacy. Our results show a satisfactory compliance with ESGE guideline, although there is still place for improvements.

Disclosure: Nothing to disclose

P1275

QUALITY OF PATHOLOGY REPORT AND ADHERENCE TO THE GUIDELINES IN A FRENCH MULTICENTER COHORT OF T1 COLORECTAL CANCER TREATED BY ENDOSCOPIC RESECTION

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Introduction: The progress made over the past ten years in therapeutic endoscopy allows treating superficial colorectal cancers with low morbidity and almost no mortality. However, lymph node involvement is found in about 10% of submucosal (T1) colorectal carcinomas, indicating additional surgical resection. According to the Japanese (JSCCR) and European (ESGE) guidelines, the presence of deep submucosal infiltration ($> 1000\mu\text{m}$), poor differentiation, lympho-vascular invasion, or grade 2-3 tumor budding should lead to additional surgery with lymph node dissection.

Therefore, each of these features has to be included in the pathology report (PR) in order to offer patients appropriate care. The aim of this study was to evaluate practices in France concerning the quality of the pathology report and the adherence to guidelines in endoscopic treatment for T1 colorectal cancers.

Aims & Methods: We conducted a retrospective study including all patients with endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) for T1 colorectal cancer performed in twelve French expert centers between March 2012 and July 2019. We collected demographic, clinical, endoscopic and histological data in order to assess: 1) the quality of the pathology report and in particular the presence of each feature requested to indicate a complementary surgery; 2) the adherence to the Japanese and European guidelines.

Results: 353 patients were included. The mean age of the population was 67.5 ± 11.0 years. 174 (49.3%) lesions were in the colon and 179 (50.7%) in the rectum. 65 (18.4%) lesions were pedunculated. 158 (44.8%) patients

had an ESD, 159 (45.0%) an EMR, 20 (5.7%) a hybrid technique, 11 (3.1%) a conventional polypectomy and 5 (1.4%) a full-thickness resection using a dedicated device (FTRD). As for the quality of the pathology reports, R0 or R1 vertical margin was indicated in 100% of cases; depth of submucosal invasion was missing in 4 (1.1%) PR; tumor differentiation was missing in 18 (5.1%) PR; tumor budding was missing in 46 (13.0%) PR; lympho-vascular invasion was missing in 18 (5.1%) PR.

Overall, at least one histological feature was missing in 57 (16.1%) PR and at least two histological features were missing in 23 (6.5%) PR. Concerning the adherence to the guidelines, additional surgery was decided in a multidisciplinary meeting in 160/346 (46.2%) patients and a simple surveillance in 186/346 (53.8%) patients, while 7 patients were lost to follow-up. 255 (73.7%) of these decisions were consistent with the guidelines.

Regarding the 91 (26.3%) patients for whom the guidelines were not followed, in most cases (85/91, 93.4%), patients had an indication for surgery according to the guidelines but a simple surveillance was proposed. 40/91 (44.0%) were not operated because the patients declined surgery or were not fit for surgery, which brings to 51/346 (14.7%) the number of patients deviating from the guidelines without justification.

Conclusion: This multicenter study indicates that 16% of pathology reports for endoscopically resected T1 colorectal cancer are incomplete and that the patient management deviates from international guidelines without justification in 15% of patients. The creation of a dedicated multidisciplinary meeting for superficial gastro-intestinal cancers in each therapeutic endoscopy center could help improving these points.

Disclosure: Nothing to disclose

P1276

A RETROSPECTIVE STUDY OF ABNORMAL FINDINGS ON COMPUTED TOMOGRAPHY (CT) AND THEIR RELATIONSHIP AND SIGNIFICANCE TO ABNORMAL ENDOSCOPY

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Introduction: Computed tomography studies are now commonplace in primary care settings in order to rule out pathology in symptomatic patients. With the advent of high definition imaging, so too has there been an increase in pathology found on CT, be it incidental or as potential cause of symptoms. Many of these patients then undergo endoscopic evaluation in order to evaluate findings on CT. In Australia, during the COVID pandemic, endoscopy to evaluate imaging findings was recognised as requiring urgent review and gastroenterologists were advised that it was reasonable to pursue endoscopic investigations within 4 to 6 weeks for this indication.

Previous studies to evaluate the correlation between bowel wall thickening (BWT) seen on CT and endoscopy, showed approximately 60% of patient would have findings at the site of BWT.

Aims & Methods: The aim of this study was to conduct a retrospective analysis of all individuals who had positive CT findings, and assess for the correlation between these positive findings and findings on endoscopy. Details of all patients who underwent endoscopic procedures (including endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP), flexible sigmoidoscopy, gastroscopy or colonoscopy) secondary to abnormal imaging studies at 2 regional hospitals (Gosford and Wyong Hospitals) in the Central Coast of New South Wales, Australia, between January 2013 to April 2020 were reviewed. These hospitals were

within the same local health district. Patient demographics, endoscopic modality, findings on endoscopy, and histopathology data were compiled. The primary endpoint was correlation between endoscopic and CT findings.

Results: From January 2013 to April 2020, there were 137 patients who underwent endoscopic investigation for the indication of abnormal CT findings. 72 were male and 65 were female. Predominant modality was colonoscopy (n=82, 59.9%), followed by gastroscopy (n=27, 19.7%), EUS (n=26, 18.9%), and ERCP (n=1, 0.7%). 2 patients underwent repeat endoscopy with a different modality (gastroscopy/colonoscopy and colonoscopy/EUS). Malignancy was found in 34 patients (24.8%) with 27 found to have adenocarcinoma, 2 with B cell lymphoma, 2 with metastatic melanoma, 1 gastrointestinal stromal tumour, 1 squamous cell carcinoma, 1 high grade neuroendocrine small cell carcinoma and 2 undefined. Polyps were found in 18 patients (13.1%) with the majority found to be tubular adenoma (n=9) followed by tubulovillous adenoma (n=4) on histopathology. 1 polyp was found to have high grade dysplasia. Diverticulosis was found to account for abnormal imaging findings in 8 patients (6.8%) In total 57 patients were found to have no significant findings on endoscopy.

Conclusion: Correlation between abnormal CT findings and findings in endoscopy was 58.4%. This suggests that there is high likelihood of finding pathology during endoscopic investigation for patients with abnormal CT findings and falls in a similar range as previous studies^{1,2}. This study supports urgent endoscopy in these patients given 24.8% of patients were found to have malignancy.

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Disclosure: Nothing to disclose

P1277

COLD PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION (EMR) FOR LARGE ADENOMAS AND SERRATED POLYPS ARE SAFE AND FEASIBLE

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Introduction: Conventional EMR carries a risk of delayed bleeding, perforation and post polypectomy syndrome. Incomplete polyp resection could lead to recurrence and post colonoscopy cancer.

Aims & Methods: Aim of the review is to report the feasibility of cold EMR for large adenomas and serrated polyps.

Methods: Prospective databases from our institution including 113 consecutive patients with 149 polyps (>1cm in size) resected by cold EMR between 2016 and 2018 were included. Demographics, clinic pathological and polyp characteristics, surveillance and recurrence data were analysed.

Results: Male: female was 2:1 with a median age of 65 years (35-83). Median polyp size was 19mm (10-40mm). one hundred and seventeen polyps (78%) were in the proximal colon. Histology of resected polyps were :47 adenomas (32%) and 102 sessile serrated polyps of which 3 had dysplasia (2.9%).

Most common sites were transverse colon (23.5%), caecum (20.8%) and ascending colon (17.4%). 78.8% of polyps were found proximal to splenic flexure.

Intra procedural oozing was witnessed during resection and settled without any haemostatic interventions in 98.6% of cases. 2 cases needed application of clips to achieve haemostasis. One patient was admitted following the procedure with abdominal pain and managed conservatively. There were no delayed bleeding or perforation. A surveillance colonoscopy (6-36 months) were carried out in 80 patients (71%) and the remainder of the patients either awaiting a planned surveillance or discharged from surveillance programme.

Overall recurrence rate following cold EMR was 3.7% (4/108) and successfully treated with cold snare resection.

Conclusion: Cold EMR for large adenomas and serrated polyps appears to be safe and feasible without any immediate or delayed complications.

Disclosure: Nothing to disclose

P1278

EFFECTIVENESS OF ORGANIZED COLORECTAL CANCER SCREENING: RESULTS FROM THE ANALYSIS OF 4001 COLONOSCOPIES PERFORMED IN PARIS BETWEEN 2015 AND 2018

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Introduction: Adenoma detection rate (ADR) is the main indicator of colonoscopy quality and is inversely proportional to post-colonoscopy colorectal cancer risk as well as colorectal cancer (CRC) mortality. French fecal immunochemical testing (FIT)-based CRC screening program recommends that ADR should be at least 45%.

Aims & Methods: The aim of this study was to assess detection rates, including ADR, within the Parisian FIT-based CRC screening program during the 2015-2018 period. ADECA 75, in charge of CRC screening in Paris area, provided all colonoscopy and pathology reports of procedures performed after a positive FIT test between April 1st, 2015 and November 15th, 2018. ADR was defined as the percentage of colonoscopies with at least one conventional adenoma (advanced or not) detected. Advanced adenoma detection rate (AADR) was defined as the percentage of colonoscopies with at least one conventional adenoma ≥ 1 cm and/or tubulovillous architecture, and/or high grade dysplasia. Proximal serrated polyp detection rate (PSPDR) was defined as the percentage of colonoscopies with at least one sessile serrated polyp/adenoma, traditional serrated polyp, hyperplastic polyps located proximally to the sigmoid colon. Adenocarcinoma detection rate was defined as the percentage of colonoscopies with at least one adenocarcinoma detected.

Results: We included 4001 colonoscopy reports performed by 396 endoscopists: 71.9% (2878/4001) in the private sector and 28.1% (1123/4001) in the public sector. At least one colorectal lesion was found in 60% (2400/4001) of the reports, with a total of 5818 lesions analyzed. Among these lesions, 61.4% were conventional adenomas, 4.7% sessile serrated polyp/adenoma, 1.7% traditional serrated polyp, 0.5% unspecified serrated lesions, 4.3% adenocarcinomas, 15.3% hyperplastic polyps, 0.5% hamartomatous polyps, 6.0% lesions with no pathology available. ADR, AADR, PSPDR and adenocarcinoma detection rates observed in the total population were respectively 48%,

6.2%, 5.7% and 5.9%. The endoscopists' individual detection rates could be determined for the 31 endoscopists who performed at least 30 colonoscopies over the study period, representing 1501 of all colonoscopies. The average ADR was 49.2 +/- 11.1% (min 23.5%, max 76.7%). ADR thresholds

of 45% and 60% were reached by 71.0% (22/31) and 16.1% (5/31) of the endoscopists. The average AADR was 5.6 +/- 7.9% (min 0%, max 35.3%). The average PSPDR was 5.3 +/- 3.2% (min 0%, max 13.3%). PSPDR thresholds of 1% and 5% were reached by 94.0% (29/31) and 51.6% (16/31) of the endoscopists. The average adenocarcinoma detection rate was 6.5 +/- 3.6% (min 0%, max 15.4%).

There was no significant difference on ADR, AADR, PSPDR and adenocarcinoma detection rate between the liberal and hospital sectors. ADR and AADR were significantly higher when colonoscopy reports were considered to be of good quality ($p < 0.001$).

Conclusion: ADR and PSPDR observed within the Parisian FIT-based CRC screening program during the 2015-2018 period were above the minimum of 45% and 1% recommended by the French Society of Digestive Endoscopy (SFED), with respectively 71.0% and 94.0% of endoscopists above these thresholds. However, there were considerable variations between endoscopists in the ADR, AADR, PSPDR and adenocarcinoma detection rates, some of them not detecting any lesion. These findings are based on about 10% of all endoscopists included. Although these results need to be confirmed in larger studies, endoscopists' awareness on the importance of sufficient detection rates is needed to improve the quality of colonoscopy service.

Disclosure: Nothing to disclose

P1279

RADIOLOGICAL WARNING SIGNS AND ACUTE DIVERTICULITIS: WHEN TO PERFORM A COLONOSCOPY?

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Introduction: Colonic diverticular disease is a very common problem in developed countries. Most guidelines recommend performing a follow-up colonoscopy 6-8 weeks after an episode of acute diverticulitis (AD) to rule out the presence of underlying colorectal cancer (CRC). However, improvement in quality and resolution of computerized tomography (CT) has questioned the role of routine colonic evaluation after AD.

Aims & Methods: The aim of this study was evaluating the correlation between the radiological findings in abdominal CT-diagnosed AD and the presence of advanced lesions in the follow-up colonoscopy, in order to determine the diagnostic efficacy of the routine colonic evaluation in these patients. Intubation rate and safety were also evaluated.

We conducted a retrospective cohort study that included all patients with AD diagnosed by CT in our Emergency Department between 2009 and 2019. The evaluated radiological findings were: colonic region, length of the affected segment and presence of fat stranding, lymphadenopathies and free intra-abdominal fluid. Endoscopic findings were classified according to the presence of advanced colonic lesion (advanced adenoma or CRC) in the corresponding CT region, diverticula as well as signs of peridiverticular inflammation. Ratios were expressed as percentages for categorical variables and for continuous variables as mean and standard deviation. Categorical variables were compared using chi-square tests applying Yates correction or Fisher's exact test. The odds ratios and their CI of 95% were also calculated.

Results: 301 patients were diagnosed of AD, of whom 103 were excluded because colonoscopy was not performed during follow up or were diagnosed by ultrasonography. 198 patients were finally included, 121 (61%) women and 77 (39%) men. Colonoscopy found 7 patients with advanced lesions (3.5%), 2 of them (1%) being CRC. Most of those lesions were identified at descendent colon compared with the rest of the colon ($p = 0.02$). Lymphadenopathies was the only radiological sign significantly related to the presence of advanced lesions in the colonoscopy (8.5%), with an OR=11,6 (95% IC: 1,4-98,7) ($p=0.02$). There were no early or delayed complications after any exploration and cecal intubation rate was 86%.

RADIOLOGICAL FINDINGS	OR	95% CI	P value
Length (< / > 5 cm)	1.1	(0.2-4.9)	$p=0.76$
Lymphadenopathies	11.6	(1.4-98.7)	$p=0.02$
Fat stranding	--	--	0.21
Intra-abdominal free fluid	1.3	(0.3-6.2)	$p>0.99$

[Association between radiological findings and advanced colonic lesion in the corresponding CT region]

Conclusion: in the absence of specific disease-wide data on CT (carcinomatosis or metastasis) and lymphadenopathies, advanced lesions detection rate was comparable to the prevalence in asymptomatic individuals aged over 50 years. Routine colonoscopy after an episode of AD should not be recommended in the absence of radiological alarm signs.

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P1280

QUALITY OF COLONOSCOPY REPORTING WITHIN AN ORGANIZED COLORECTAL CANCER SCREENING PROGRAM: AN ANALYSIS OF 4001 REPORTS FROM PARIS BETWEEN 2015 AND 2018

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Introduction: Several quality assurance guidelines for colonoscopy have been published at a national and international level for the past years. The recent 2018 guidelines from the French Society of Digestive Endoscopy (SFED) have proposed major (essential) and minor quality indicators for colonoscopy procedure and report. To date, data on the quality of colonoscopy reporting is scarce.

Aims & Methods: The aim of this work was to evaluate the quality of colonoscopy reporting in Paris area within the French fecal immunochemical testing (FIT)-based CRC screening program during the 2015-2018 period.

ADECA 75, in charge of CRC screening in Paris area, provided all colonoscopy and pathology reports of procedures performed after a positive FIT test between April 1st, 2015 and November 15th, 2018. Colonoscopy reports were analyzed according to administrative, regulation and medical criteria established by the 2018 SFED guidelines. We evaluated a global quality score for colonoscopy reporting, including 5 of the 6 major per-procedure quality indicators of the French guidelines: anesthesia modalities, bowel preparation quality according to Boston Bowel Preparation Scale (BBPS), documentation of cecal landmarks, macroscopic appearance of colorectal lesions and description of lesion removal techniques.

Results: Of the 4001 colonoscopies included, 71.9% (2878/4001) were performed in the private sector and 28.1% (1123/4001) in the public sector. Procedure indication was found in 93.6% of cases (3744/4001) but only 30.2% (1207/4001) of reports mentioned a positive FIT test. Bowel preparation quality was reported qualitatively in 83.1% (3324/4001) of cases whereas the BBPS was used only in 59.0% (2361/4001) of the reports. Colonoscopy completeness was reported in 96.1% (3843/4001) of cases. Colonoscopy withdrawal time was indicated in 8.7% (3843/4001).

Number, macroscopic appearance, location and size of colorectal lesions were described in respectively 100% (5818/5818), 63.3% (3683/5818), 99.1% (5765/5818), and 86.2% (5017/5818). Paris and Kudo classification were used in respectively 2.3% (133/5818) and 0.4% (21/5818) of reports. Description of lesion removal techniques was found in 72.5% (4219/5818) cases. Complications were described in 2.2% (89/4001) reports. Recommendations for follow-up were indicated in 33.8% (1351/4001). Photodocumentation of cecal landmarks or lesions were present in respectively 3.7% (147/4001) and 4.4% (176/4001).

Reports were considered of good quality if at least 4 of the 5 major criteria were present, which happened in 73.6% (1766/2400). Good quality reports were more frequent at the 2017-2018 period compared to the 2015-2016 period (76.8% vs. 70.3%, $p < 0.001$).

Conclusion: Colonoscopy reporting was considered to be of good quality in almost three-quarters of cases (73.6%) and improved between 2015 and 2018. Main weaknesses of reporting were related to the type of bowel preparation used, BBPS use, colonoscopy withdrawal time, macroscopic appearance description of colorectal lesions and photodocumentation of the procedure. Adoption of a standardized electronic report at a national and international level appears to be necessary to achieve optimal reporting for a better quality of the colonoscopy service.

Disclosure: Nothing to disclose

P1281 WITHDRAWN

P1282

FIRST RESULTS USING SPEEDBOAT TUNNELING TECHNIQUE IN COLORECTAL SUBMUCOSAL DISSECTION: CLINICAL OUTCOMES AND PROCEDURE TIME PREDICTION MODELS

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Introduction: The 'Speedboat-RS2/SRS2' (Creo-Medical/Wales/UK) is the first multi-modality device, incorporating bipolar-radiofrequency/BRF energy cutting, microwave-coagulation/MWC, an integrated needle for submucosal injection and a rotatable blade with a heat-insulated hull.

Aims & Methods: A prospective database of endoscopic submucosal dissection cases/ESD using the SRS2 device was initiated from June 2018 to Dec 2019. Two experienced operators performed all cases. Short and long-term clinical outcomes were recorded. Linear regression was used to explore whether factors, such as polyp size/location/morphology could predict the duration of the procedure in minutes, using submucosal tunneling.

Results: Sixty-nine patients were subject to colorectal ESD using submucosal tunneling technique, 55 under conscious sedation and 14 general anaesthesia. Five cases were abandoned; 3 with advanced cancer and 2 who developed uncontrolled hypertension despite sedation. Out of 64 patients an endoscopically complete en-bloc resection was achieved in 83% (n=53) and the curative resection rate was 77% (n=49). Conversion to piecemeal snare resection occurred in 17% (n=11) due to lack of scheduled procedure time in 6, and device related issues in 5. Overall median polyp size was 4cm (range 1-12cm), non-rectal polyps 30/64 (47%), granular polyps 46/64 (72%), polyps with high grade dysplasia 18/64 (28%) and polyp cancers in 8/64 (12.5%). Five T1 cancers with < 1000µm depth of invasion and no adverse histology features had no recurrence at follow up endoscopy (4/5) or surgery (1/5). Three T1 cancers with < 1000µm depth of invasion but with adverse histological features opted for conservative management due to advanced age and no endoscopic recurrence was seen. Overall the first surveillance endoscopy was available in 23/64 (36%) patients and zero recurrence was identified. Microwave energy was utilized to pre-coagulate and control active bleeding in most cases. Hemostatic monopolar forceps were required in 8/64 (12.5%) cases. Endoscopically controlled delayed bleeding occurred in 4 patients (6.2%), half of those in the conversion to snare group. Mild post polypectomy syndrome was experienced by 3/64 (4.7%) patients. Only 3/53 (5.6%) episodes of muscle injury were seen in the en-bloc group, requiring no intervention. No perforation was recorded.

Overall median time of the procedure was 90mins (range 15-270mins). Three statistical models were used to determine the predictive value of the procedure time using different factors such the polyp size, polyp morphology and polyp location. In all models, there was significance on polyp size ($p < .001$, $R^2 = .227$), indicating an increase of 10.15 minutes per 1cm of increase in polyp size.

Constant (CI)	44.84 (18.40, 71.28)	13.17	.001
Polyp size (CI) cm	10.15 (4.89, 15.4)	2.62	<.001

[Effects of Polyp Size in Procedure Time]

The polyp location was added as second predictor and the 2nd model was significant ($p < .001$, $R^2 = .253$), indicating a trend of a faster dissection rate for rectal polyps. A further third predictor, polyp morphology, was included and the 3rd model was significant ($p < .001$, $R^2 = .285$), indicating a trend of a slower dissection rate on the granular polyps.

Conclusion: These first results demonstrated that Speedboat SRS2 is a safe device for submucosal tunneling and an acceptable ESD device. In addition, polyp size predicts an increased procedure time as may polyp location beyond the rectum and granular morphology.

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P1283

ABLATION AND COLD AVULSION (ACA) FOR THE MANAGEMENT OF NON-LIFTING SCARRED COLORECTAL LESIONS

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Introduction: A scarred submucosa limits the effectiveness of lifting during endoscopic mucosal resection (EMR) and may necessitate surgery. Endoscopic submucosal dissection (ESD) of scarred lesions is technically difficult and carries a significant risk of perforation. We report our experience of a salvage approach using ablation and cold avulsion (ACA) as an adjunct to EMR.

Aims & Methods: Lesions treated with ACA between January 2015 - October 2019 were identified from a retrospective database. Following EMR, residual areas of non-lifting scarred tissue were ablated using high power argon plasma coagulation (APC). The cauterised polyp tissue was then avulsed using non-spiked biopsy forceps. Surveillance endoscopies and histology reports were reviewed and evidence of polyp recurrence documented. Recurrence was treated with repeat ACA.

Results: Eighty-six patients (male n=47, mean age 69 years, range 49-86) with 88 polyps (median size 36.6mm, range 10-120mm) underwent ACA. Thirty-eight (43%) lesions were located proximal to the transverse colon. Forty-two lesions (47.7%) were recurrent lesions. The remaining 46 (52.3%) were partially non-lifting, de novo lesions.

Intraprocedural bleeding requiring treatment with haemostatic forceps occurred in 12 cases (13.6%) during snare resection, although areas treated with ACA never required treatment with haemostatic forceps or clips. Intraprocedural perforation occurred in one case (target sign) during snare resection and was successfully closed with endoscopic clips prior to ACA. No perforation was reported during ACA.

Following the index ACA procedure, histology showed: adenoma with low grade dysplasia in 63.6% (n= 56); high grade dysplasia in 30.7% (n= 27); serrated lesions without dysplasia in 4.5% (n=4). One patient had a moderately differentiated adenocarcinoma and subsequently declined surgery with no endoscopic evidence of recurrence at 24 months.

Endoscopic follow-up was available for 78 lesions (mean 13.4 months, range 3-60). Recurrence at first follow-up was 30.7% (24/78). Follow-up for the second and third procedure was available for 17 patients with clearance rates of 58.8% (10/17) and 42.8% (3/7) respectively. Of the remaining 4 patients with recurrence, 3 underwent surgery (adenoma with low grade dysplasia n= 2, progression from high grade dysplasia to T1 adenocarcinoma n= 1). One was lost to follow-up following the development of significant co-morbidity.

Conclusion: The endoscopic clearance rate using ACA was 95.7%. ACA appears to be a safe, effective, and surgery-sparing therapy in this difficult cohort of, scarred, partially non-lifting lesions.

Disclosure: Nothing to disclose

P1284

THE IMPACT OF ENDOSCOPIC SUBMUCOSAL DISSECTION ON THE COMPLEX POLYP SERVICE

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Introduction: Endoscopic excision of complex polyps is a rapidly evolving treatment, and particularly endoscopic submucosal dissection (ESD) might represent an option for superficial malignant submucosal invasion. Limited data is available in western series for clear indications for ESD.

Aims & Methods: We prospectively collected data between January 2017 and December 2018 of excision of complex polyps. We compared short term outcomes data between piecemeal and en-bloc excisions between 2017 and 2018, and outcomes in endoscopically resected polyps that were incidentally found to be malignant.

Results: 189 patients (80 females, mean age 69.9, sd 11.8) underwent 207 polypectomies. Of these, in 124 we employed a piecemeal technique, and en-bloc resection in 83 (41 EMR en-bloc and 42 ESD; 13 of which were performed in 2017 and 29 in 2018). There was no difference in the rates of complications between the en-bloc and the piecemeal groups. We experienced no perforation or need for transfusion in either group. In 8 patients (6.5%) of the piecemeal group there was polyp recurrence, whilst no recurrence was seen in the en-bloc group.

Histology showed cancer in 14 specimens within the en-bloc group. Out of these, 10 patients underwent surgical resection, and residual cancer was found only in one case. In the other 4 patients endoscopic surveillance showed no recurrence. Histology confirmed cancer in 6 patients within the piecemeal group. Of these, 3 underwent surgical resection and 3 patients were subject to endoscopic surveillance with one recurrence.

Conclusion: In our cohort, en-bloc resections appeared to be as safe as piecemeal polyp resections, but with lower recurrence rates. In our practice, rates of ESD increased two-fold over the 2 year period, and it might represent a treatment option for superficial submucosal malignant invasion. Future studies are warranted to address the role of ESD for polyp cancers.

Disclosure: Nothing to disclose

P1285

THE COLON ENDOSCOPIC BUBBLE SCALE (CEBUS): A RELIABILITY STUDY

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Introduction: To date no scale has been validated for assessing bubbles impairing bowel preparation, leading to the use of different descriptions in randomized trials limiting clinical interpretation. Therefore, our goal was to develop and determine reliability of the Colon Endoscopic Bubble Scale - CEBuS.

Aims & Methods: Multicentre prospective observational study with 2 on-line evaluation phases (1. evaluation by 4 expert endoscopists; 2. mix of 6 expert and 13 non-expert) of 45 still colonoscopy images (15 per scale level), randomly distributed. Images were assessed twice with a two-week interval a) using the CEBuS scale (0 if no or minimal amount of bubbles, covering < 5% of the surface; 1 - bubbles covering 5-50%; 2 - bubbles covering >50%); and b) for possible clinical attitude (do nothing; wash with water; wash with simethicone).

Results: Twenty-three observers (10 experts and 13 non-experts), from ten endoscopy units, participated with 100% response rate. An overall almost perfect interobserver reliability (ICC=0.92, 95%CI 0.89-0.95) and substantial intraobserver reliability (Kappa=0.77, 95%CI 0.75-0.78) was observed. Results were similar in phase 1 and 2 (ICC 0.92, 95% CI 0.87-0.95 vs. 0.93, 95%CI 0.91-0.96; Kappa 0.74, 95%CI 0.65-0.81 vs. 0.79, 95%CI 0.77-0.81). Comparing experts (n=10) versus non-experts (n=13) the CEBuS performed with a near-perfect interobserver reliability in both groups (ICC 0.90, 95%CI 0.86-0.94 vs. 0.94, 95%CI 0.91-0.96) and a substantial intraobserver reliability (Kappa 0.75, 95%CI 0.71-0.78 vs. 0.79, 95%CI 0.76-0.81). Agreement on clinical attitude was moderate (Kappa 0.55, 95%CI 0.55-0.56), resulting from a low percent positive agreement in CEBuS-1 images (21%, 16-26).

Conclusion: The CEBuS proved to be a valid and reliable instrument to standardise the evaluation of colonic bubbles during colonoscopy.

Disclosure: Nothing to disclose

P1286

LONG-TERM OUTCOMES OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN DIFFICULT LOCATIONS: DENTATE LINE, ILEOCECAL VALVE AND CECUM

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Introduction: Endoscopic resection of tumors at the perineal rectum extending to the dentate line (RTDL) and ileocecal valve (ICV) and cecum is difficult due to either the narrowness of the lumen and nonlinear anatomy that hinders visualization and instrumental maneuvering.

Aims & Methods: Aim to assess ESD outcomes in difficult locations. Prospective single center European study conducted from January 2013 to November 2018. All consecutive superficial neoplasms >20 mm or with a positive no-lifting sign secondary to a previous resection in the perineal rectum either involving the dentate (the distal margin within 10 mm from the dentate line) or not, the ICV (eventually invading the terminal ileum), the cecum, and ascending colon.

Outcomes (en bloc, R0 and recurrence rates) were compared in adjacent segments. ESD was performed by the standard technique by an expert operator (case volume prior the study: 80 procedures). Residual rate was assessed at least after 12 months.

Results: Tumor features and ESD outcomes are reported in the Table. Prevalence of scarring neoplasm was higher in rectal and ICV groups; although, no significant differences were observed in patient and neoplasm features. RTDL distal margin was at the squamous epithelium of the dentate line in 32 cases. Ileal extension was observed for 8 (29%) cases.

En bloc and R0 resection rates for RTDL and pelvic rectal tumors were not significantly different. However, residual rate was significantly higher in RTDL (P=0.002). ESD en bloc and R0 rate for ICV, cecal, and ascending colon tumors were not significantly different, as well as residual rate.

	RTDL n.50	Pelvic R n.92	ICV n.27	Cecum n.67	Ascending Colon n.118
Size (mm), median (range)	44 (15-180)	32 (14-95)	31 (15-85)	33 (15-60)	39 (15-115)
Scar presence, n. (%)	9 (18)	11 (12)	5 (19)	4 (9)	10 (8)
Morphology: LST- NG/G, n. (%)	3 (6) / 40 (80)	12 (13) / 61 (66)	4 (15) / 19 (83)	9 (19) / 35 (74)	21 (18) / 91 (77)
Operation speed, cm2/min	0.10 (0.01-0.37)	0.07 (0.00-0.55)	0.07 (0.02-0.18)	0.11 (0.01-0.40)	0.16 (0.00-0.82)
Perforation, n. (%)	0	1 (1)	0	1 (1)	1 (1)
En bloc / R0, n. (%)	41 (82) / 38 (76)	82 (89) / 75 (82)	24 (88) / 21 (78)	39 (83) / 39 (83)	106 (90) / 106 (90)
Curative, n. (%)	33 (66)	75 (82)	24 (88)	38	101
Residual, n (%)	4 (12)	0	2 (7)	1 (3)	1 (1)

[Tumor features and ESD outcomes]

Conclusion: ESD for RTDL and cecal tumors shows lower en bloc resection rates compared to adjacent colorectal segments, but the procedure was similarly feasible and safe regardless a higher scar prevalence of previous

resections. The narrowness of the perineal rectum at the anal canal and the nonlinear ICV anatomy are associated to clinically relevant residual rates, therefore and follow-up within 12 months is advisable for these locations.

Disclosure: Nothing to disclose

P1287

POLYPECTOMY REFERRAL TO EXPERTS DEPENDS ON THE ENDOSCOPIST'S SETTING NOT THE SPECIALISATION

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Introduction: The ESGE-Guidelines for colorectal polypectomy propose an algorithm upon which polyps should be referred to expert centers for polypectomy. There is little knowledge about the real situation concerning referrals to tertiary centers for polypectomy. Therefore, our aim of the study was to assess the rates and size of referred polyps according to endoscopist's specialty and setting.

Aims & Methods: Screening colonoscopies from the years 2007-2019 were analyzed within Austrian Certificate in Quality for Screening Colonoscopy. We evaluated the rate of polyps referred to expert centers for polypectomy according to polyp's size and compared these rates in relation to endoscopist's specialty and setting. Polyp's size was described as < 5 mm, 0,5-1 cm, 1-2 cm and >2 cm.

Results: Polyps were found in 131 483 screening colonoscopies, 62,62% were performed by internists, 32,89% by surgeons and 4,49% interdisciplinary. According to setting, 73,37% were performed in private practices, 23,78% in hospitals and 2,85% in outpatient clinics. Mean polyps' rate referred for polypectomy was 18,45% (SD=29,81) for internists, 17,36% (SD=28,30) for surgeons and 13,28% (SD=23,05) in the interdisciplinary group; 21,48% (SD=31,61) for private practices, 7,94% (SD=16,36) for hospitals and 25,37% (SD=36,92) for outpatient clinics.

No statistical difference was found between the rates of internists and surgeons (polyps < 5mm: p=0,714; polyps 0,5-1cm: p=0,256; polyps 1-2 cm: p=0,691; polyps >2cm: p=0,683).

There was also no significant difference between internists and the interdisciplinary group (polyps < 5mm: p=0,681; polyps 0,5-1cm: p=0,514; polyps 1-2 cm: p=0,550; polyps >2cm: p=0,471).

Between surgeons and the interdisciplinary group no statistical difference could be found (polyps < 5mm: p= 0,605, polyps 0,5-1cm: p=0,834; polyps 1-2 cm: p= 0,656; polyps >2cm: p=0,361).

Statistical difference could be shown between the rates of private practices and hospitals (polyps < 5mm: p=0,035; polyps 0,5-1cm: p < 0,001; polyps 1-2 cm: p < 0,001; polyps >2cm: p < 0,001).

There was no significant difference between private practices and outpatient clinics (polyps < 5mm: p=0,690; polyps 0,5-1cm: p=0,432; polyps 1-2 cm: p=0,853; polyps >2cm: p=0,416).

Between hospitals and outpatient clinics statistical difference was found only for polyps >2cm: p=0,038; (polyps < 5mm: p= 0,936, polyps 0,5-1cm: p=0,231; polyps 1-2 cm: p= 0,300).

Mean polyps' rate referred for polypectomy	Polyp's size			
	<5mm	0,5-1cm	1-2 cm	>2cm
Internists	1,48% (SD=7,24)	6,46% (SD=12,37)	25,16% (SD=30,66)	42,62% (SD=37,94)
Surgeons	1,19% (SD=3,74)	4,80% (SD=10,21)	23,65% (SD=28,94)	44,65% (SD=35,58)
Interdisciplinary group	0,65% (SD=1,05)	4,19% (SD=6,3)	19,75% (SD=24,69)	33,77% (SD=33,21)
Private practices	1,67% (SD=7,28)	7,05% (SD=12,93)	29,32% (SD=32,18)	51,39% (SD=36,45)
Hospitals	0,60% (SD=0,89)	2,24% (SD=3,59)	11,40% (SD=15,74)	19,01% (SD=25,59)
Outpatient clinics	0,57% (SD=0,90)	11,00% (SD=17,38)	27,02% (SD=36,29)	62,89% (SD=43,71)

[Mean polyps' rate referred for polypectomy according to polyp's size]

Conclusion: The study showed that significantly more polyps according to all polyps' sizes were referred to expert centers for polypectomy by private practices than hospitals and more polyps >2cm were referred to expert centers for polypectomy by outpatient clinics than hospitals.

There was no significant difference in referring polyps to expert centers for polypectomy according to endoscopist's specialty.

Disclosure: Nothing to disclose

P1288

BIOSIGNALS DURING SEDATION IN COLONOSCOPY AND THE RELATIONSHIP WITH THE SATISFACTION OF THE CLINICIAN WITH THE SEDATION

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Introduction: Nurse assisted propofol sedation (NAPS) is a common and safe method for performing colonoscopy. Although appreciated by patients, little is known about the factors that negatively influence the satisfaction of endoscopists performing colonoscopy with NAPS. In this study, we aim to correlate observer reported pain events to clinician satisfaction with the examination. Additionally, we aimed to identify patient biosignals during endoscopy, which correlate with those events and are able to objectively predict them.

Aims & Methods: Consecutive patients scheduled for a colonoscopy with the use of NAPS were prospectively recruited. During the examination observer reported pain events including movements and paralinguistic sounds were simultaneously recorded with different biosignals (including facial electromyogram (EMG), skin conductance level, and electrocardiogram). After the procedure, the examiners filled out the Clinician Satisfaction with Sedation Instrument (CSSI). Primary endpoint was the correlation between CSSI and observer reported pain events and the identification of biosignals that are able to predict those events. Secondary endpoints included correlation between CSSI and sedation depth, frequency and dose of sedative use, polyps resected, resection time, duration of the examination and time to reach the cecum and the experience of the nurse performing NAPS. ClinicalTrials.gov identifier: NCT03860779

Results: 112 patients with 98 (88.5%) available biosignals were prospectively recruited. There was a significant correlation between an increased number of observer reported pain events during endoscopy with NAPS and a lower CSSI ($r = -0.318$, $p = 0.001$).

Additionally, EMG-signal of facial muscles correlated best with the event time points and the signal was able to significantly rise above baseline 30 seconds prior to the event of paralinguistic sounds. Secondary endpoints presented that propofol dose relative to the examination time, coecal intubation time, the time spent on polyp removal, and the individual nurse performing the NAPS significantly correlated with CSSI.

Conclusion: This study presents that movements and paralinguistic sounds during endoscopy negatively correlate with satisfaction of the examiner measured by CSSI. Additionally, EMG of facial muscles is able to identify such events and possibly is able to predict their occurrence.

Disclosure: Nothing to disclose

P1289

NON-INVASIVE COLORECTAL NEOPLASMS REFERRED TO SURGERY: A PERFORMANCE KEY MEASURE FOR SCREENING PROGRAMS

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Introduction: Performance key measures of endoscopic resection have not yet been defined. A second-look colonoscopy reclassify a large proportion of neoplasms as superficial and amenable of curative endoscopic resection that otherwise would have undergone unnecessary surgery. Heterogeneity operator competency and a patchy access to advanced resection techniques can have unfavorable impacts on colorectal cancer screening.

Aims & Methods: Observational, multicenter study including all consecutive patients referred to surgery for a colorectal neoplasm from all screening centers in a region of central Italy within a 2-year period. Data were retrieved from county registry and crosschecked with prospectively collected charts from the databases of individual centers. Cancers were defined at endoscopy as superficial (Paris class) or deep (Borrmann class). Noninvasive cancer definition: not invading the submucosa (SM) either on endoscopic or surgical specimens.

Primary outcomes: noninvasive cancer rate according to endoscopic staging and resection (ER). Secondary outcome: indefinite cancer diagnosis at histology of ER specimens due to lack of SM invasion reporting or indefinite microstaging of T1 cancer with free vertical margin.

Results: A total of 468 neoplasms from 13 centers were included. Patients were 64 y.o. (range 56-74), 256 males (58%). Neoplasms were superficial in 188 cases and deep in 280. Superficial neoplasms underwent ER (Sup-ER) in 92 (49%) and biopsies in 96 (Sup-B) (51%). Sup-ER were smaller ($P < 0.0001$), more frequently pedunculated ($P < 0.0001$), and in the left colon ($P < 0.0001$) than Sup-B. ER was complete in 76 (83%): en bloc in 45 (59%), piecemeal in 31 (41%). Complete resection was achieved in smaller ($P = 0.006$) and more frequently pedunculated neoplasms ($P = 0.043$).

Overall noninvasive cancer rates of Sup-ER, Sup-B and Deep-B were 10%, 40% and 9%, respectively (Table). Sup-B noninvasive cancer rate was significantly higher than Sup-ER group ($P < 0.01$); ulcer-negative Deep-B rate was significantly higher than ulcer-positive and stricturing Deep-B ($P = 0.0002$). Indefinite cancer rate was significantly higher in Sup-ER with incomplete resection ($P = 0.012$). Performance of endoscopic centers was significantly different: noninvasive cancer rate ranged from 0% to 30% ($P = 0.0581$), in particular in Sup-B ranged from 0% to 100% ($P = 0.019$). Prevalence of non-invasive cancers was $< 10\%$ in 5 centers and $> 20\%$ in 5.

	Sup-ER			Sup-B		Deep-B	
	En bloc n.45	Piece- meal n.31	Incom- plete n.16	n.96	Ulcer- neg n.76	Ulcer- pos n.130	Stricture n.74
Noninvasive, n. (%)	2 (4)	5 (16)	3 (19)	38 (40)	15 (20)	7 (5)	2 (3)
Indefinite ca diagnosis, n. (%)	8 (18)	7 (23)	8 (50)	n.a.	n.a.	n.a.	n.a.
SM invasion not reported	1 (2)	3 (10)	6 (38)	-	-	-	-
T1 microstaging incomplete	7 (16)	4 (13)	2 (13)	-	-	-	-

[noninvasive cancer rates of Sup-ER, Sup-B and Deep-B]

Conclusion: The overall prevalence of noninvasive cancers referred to surgery in the present cohort study based a organized screening program is 15%. However, performance is widely heterogeneous among different centers due to significantly different rates in superficial neoplasms not underwent ER and deep neoplasms without invasive features (i.e. stricture or ulceration). Present results suggest that corrective actions should be: improvement in endoscopic neoplasm characterization in all centers; identification of centers for endoscopic resection were advanced techniques should be available (i.e. ESD) and that should be interrogated before surgery referral. The rate of noninvasive cancers referred to surgery should be integrated in screening programs being as relevant as the adenoma detection rate.

Disclosure: Nothing to disclose

P1290

INFLUENCE OF ARTIFICIAL INTELLIGENCE ON POLYP DETECTION IN A REAL LIFE SCENARIO

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Introduction: Commercially available polyp detection systems for colonoscopy using artificial intelligence (AI) techniques were recently introduced. Although studies present that AI helps to increase the number of detected polyps, it is not clear if just the presence of the AI system leads to a more vigorous examination of the colonic mucosa, for example due to the appearance of false positive polyp detections. Additionally, the published studies do not report on how stable an AI-signal should be before it can be regarded as true positive.

Aims & Methods: In this work we intend to identify changes of polyp rate (PR) with and without the use of AI and subsequently analyze true positive and false positive detection rates of AI on an in depth frame-by-frame basis.

Colonoscopies of consecutive patients were performed in two centers with and without the use of a commercially available AI system (GI Genius, Medtronic). Exclusion criteria for the analysis were distal colonic stenosis, poor visualization of the mucosa and inflammatory bowel disease. Primary endpoint was the difference of PR defined by all identified polyps relative to the number of colonoscopies with and without the use of the AI system. Secondary endpoints included the analysis of all AI-detections in a subset of 12 colonoscopies calculating true positive and false positive detection rates on a frame-by-frame based analysis (ClinicalTrials.gov identifier: NCT04335318).

Results: Out of the 122 examinations without AI 75 were included compared to 105 of the 126 examinations with the use of AI. The PR without AI was 0.92 compared to 0.85 with the help of AI. The in depth analysis of the AI performance in a subset of 12 colonoscopies presented that 8 out of 9 polyps were identified by the AI in minimum one single frame. Regarding the total number of frames where each single polyp was visible, the AI detected it in median 35.4% (range 3.3 to 87.7%). Additionally, the time from the first appearance of the polyp until recognition by the AI was median 1.6 seconds (range 0.2 to 8.6 seconds). False positive AI-detections were median 297.5 frames (range 54 to 590 frames) per colonoscopy.

Conclusion: The commercially available AI we tested had no profound effect on the PR in this work. Still, the AI detected the majority of the polyps in the in depth analyzed subset. However, due to the high number of false positives and the fact that polyp detection was not consistent during the time the polyp was visible, a major effect of AI might be to increase the respective examiner's vigilance level due to appearance of multiple detection boxes rather than AI-based detection of polyps per se.

Disclosure: Nothing to disclose

P1291

ARE THE EUROPEAN GUIDELINES ON POLIPECTOMY TECHNIQUES IN A TERTIARY ONCOLOGIC ENDOSCOPY UNIT APPLIED? YES OR NOT?

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Introduction: The endoscopic removal of colorectal polyps is considered an essential skill for an endoscopist who perform colonoscopies. European Society of Gastrointestinal Endoscopy (ESGE) guidelines suggest a specific approach depending on the different kind (sessile or pedunculated) and size of polyps. Post-polypectomy surveillance is influenced by a correct removing of precancerous lesion with an impact on cost and comfort of patients whose often need to underwent surveillance more frequently then scheduled. According to ESGE guidelines, sessile polyps under 3 millimeters can be removed by biopsy forceps, whereas from 4 mm to 9 mm must be removed by cold snare and by hot snare over 9 mm.

Aims & Methods: We evaluated the application of ESGE guidelines about polypectomy techniques in our Endoscopy unit. Data on colonoscopies performed since June in the 2019 until December in 2019 in an Endoscopy Unit of Italian Oncologic tertiary center were retrospectively analyzed. Each exam was classified as correct if the polypectomy techniques proposed by ESGE guidelines were followed and wrong if at least one of multiple polypectomies in the same colonoscopy did not agree with guidelines. Sessile polyps under 3 mm removed using biopsy forceps, sessile polyps under 9 mm with cold snare and over 9 mm with hot snare were considered correct procedures. The cutting of pedunculated polyp with hot snare after submucosal lifting was considered correct polypectomy too.

Results: In a preliminary analysis, We considered 969 colonoscopy. 504 (52%) colonoscopy were rule out because without polypectomy. Among colonoscopy with polypectomy in 217 cases out 465 (47%), at least one polypectomy was performed in a wrong way. Moreover, only 1,1% (2/175) of 4 mm sessile polyp was removed by cold snare and not by biopsy forceps. All pedunculated polyps were removed in the correct way.

Conclusion: Fifty-two percent of polypectomies in our unit were performed not in agreement with European guidelines. The 3 mm cutoff for the use of biopsy forceps was not perceived as mandatory and so there was not a different approach between 3 and 4 mm polyps. At same time, we speculated that today is there not a standardized and precise manner to measure polyp size, so the 3 mm cutoff could be considered arbitrary. However further investigation, a complete analysis on our cases and a comparison with other endoscopy unit experiences will be necessary to confirm this preliminary evidence and the reason of no adherence to guidelines.

Disclosure: Nothing to disclose

P1292

DEVELOPMENT AND VALIDATION OF AN INTERACTIVE TRAINING MODULE TO OPTICALLY DIAGNOSE COLORECTAL POLYPS USING OF THE WORKGROUP SERRATED POLYPS AND POLYPOSIS (WASP) CLASSIFICATION WITH PENTAX ISCAN OPTICAL ENHANCEMENT (OE) TECHNIQUE

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Introduction: In 2016, the Workgroup Serrated Polyps and Polyposis (WASP) developed a classification system for endoscopic differentiation of adenomas, hyperplastic polyps (HPs) and sessile serrated lesions (SSLs). As it was developed for use with narrow band imaging (NBI) and never evaluated for other virtual chromoendoscopy techniques, we investigated whether the WASP classification could also be used with the Pentax iScan optical enhancement (OE) system.

Aims & Methods: A training session was organized, in which 11 senior endoscopists and 10 junior endoscopists participated. During this session, characteristics of different types of diminutive polyps using white light and different iScan settings (including OE) were discussed. Before and after this session (T₀ and T₁), the participants were invited to score polyp histology, including levels of confidence, of 30 short videos of diminutive polyps. After three months, the same endoscopists were invited to score a new set of 30 videos (T₂). The primary outcome was the overall diagnostic accuracy at T₀, T₁ and T₂. Secondary outcomes were the specific accuracy specifically for adenomas, SSLs and neoplastic versus non-neoplastic lesions.

Results: Diagnostic accuracy of all polyps was 0.57 (IQR 0.50-0.60) at baseline, which had improved to 0.60 (IQR 0.50-0.67, p=0.135) after training. For polyps diagnosed with high confidence, accuracy was 0.65 (IQR 0.55-0.72) at baseline, which improved to 0.67 (IQR 0.58-0.72, p=0.267) after training. Diagnostic accuracy for SSLs was 0.41 (IQR 0.35-0.47) at baseline, which improved to 0.47 (IQR 0.41-0.53) after training. For SSLs diagnosed with high confidence, accuracy was 0.38 (IQR 0.30-0.51), which significantly improved to 0.50 (IQR 0.40-0.55, p=0.009) after training. After three months, overall diagnostic accuracy remained 0.60 (IQR 0.57-0.65, p=0.266). Additionally, the diagnostic accuracy for SSLs was 0.50 (IQR 0.44-0.59, p=0.049) and 0.50 (IQR 0.38 - 0.57, p = 0.039) for all SSLs and SSLs diagnosed with high confidence, respectively.

	T0, accuracy (IQR)	T1, accuracy (IQR)	T2, accuracy (IQR)
Overall	0.57 (0.50 - 0.60)	0.60 (0.50 - 0.67)	0.60 (0.57 - 0.65)
Overall - HC	0.65 (0.55 - 0.72)	0.67 (0.58 - 0.72)	0.65 (0.59 - 0.71)
Neoplastic vs. non-neoplastic	0.58 (0.54 - 0.65)	0.62 (0.52 - 0.67)	0.61 (0.58 - 0.65)
Neoplastic vs. non-neoplastic - HC	0.64 (0.53 - 0.71)	0.65 (0.57 - 0.74)	0.67 (0.62 - 0.71)
SSL vs. non-SSL	0.41 (0.35 - 0.47)	0.47 (0.41 - 0.53)	0.50 (0.44 - 0.59)*
SSL vs. non-SSL - HC	0.38 (0.30 - 0.51)	0.50 (0.40 - 0.55)*	0.50 (0.38 - 0.57)*
Adenoma vs. non-adenoma	0.89 (0.78 - 1.00)	0.89 (0.72 - 1.00)	0.80 (0.75 - 0.80)*
Adenoma vs. non-adenoma - HC	1.00 (0.85 - 1.00)	1.00 (0.85 - 1.00)	0.89 (0.29 - 1.00)

[Table 1 Changes in accuracy at T0, T1 and T2. IQR interquartile range; HC high accuracy; SSL sessile serrated lesion; *significant improvement.]

Conclusion: Although participation in a training module for the WASP classification using Pentax iScan OE system did not improve the overall diagnostic accuracy of optical diagnosis of colorectal polyps, it significantly improved the diagnostic accuracy of SSLs, especially when diagnosed with high confidence.

Disclosure: Nothing to disclose

P1293

A RANDOMIZED CONTROLLED TRIAL OF AN EDUCATIONAL VIDEO TO IMPROVE QUALITY OF BOWEL PREPARATION FOR COLONOSCOPY

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Introduction: High-quality bowel preparation is necessary for colonoscopy. A few studies have been conducted to investigate improvement in bowel preparation quality through patient education. However, the effect of patient education on bowel preparation has not been well studied.

Aims & Methods: The aim of this study was to measure the effect of a simple video on the quality of bowel preparation during colonoscopy and its impact on clinically relevant outcomes, such as polyp detection. In addition, we investigated factors associated with poor bowel preparation.

A randomized and prospective study was conducted. All patients received regular instruction for bowel preparation during a pre-colonoscopy visit. Those scheduled for colonoscopy were randomly assigned to view an educational video instruction (video group) on the day before the colonoscopy, or to a non-video (control) group. Qualities of bowel preparation using the Ottawa Bowel Preparation Quality scale (Ottawa score) were compared between the video and non-video groups. In addition, factors associated with poor bowel preparation were investigated.

Results: A total of 168 patients were randomized, 88 to the video group and 80 to the non-video group. The video group exhibited better bowel preparation (mean Ottawa total score: 3.03 ± 1.9) than the non-video group (4.21 ± 1.9; P<0.001) and had good bowel preparation for colonoscopy (total Ottawa score < 6: 91.6 % vs. 78.5 %; P<0.001). Multivariate analysis revealed that males (odds ratio [OR] = 1.95, P = 0.029), diabetes mellitus patients (OR = 2.79, P = 0.021), and non-use of visual aids (OR = 3.09, P<0.001) were associated with poor bowel preparation. In the comparison of the colonoscopic outcomes between groups, the polyp detection rate was not significantly different between video group and non-video group (48/250, 19.2 % vs. 48/252, 19.0 %; P = 0.963), but insertion time was significantly short in video group (5.5 ± 3.2 min) than non-video group (6.1 ± 3.7 min; P = 0.043).

Conclusion: The addition of an educational video could improve the quality of bowel preparation in comparison with standard preparation method.

Disclosure: Nothing to disclose

P1294

EFFECTIVENESS AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTROINTESTINAL LESIONS WITH SIGNIFICANT SUBMUCOSAL FIBROSIS: A WESTERN PROSPECTIVE COHORT STUDY

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Introduction: Endoscopic submucosal dissection (ESD) is used for 'en-bloc' resection of superficial gastrointestinal neoplasms regardless of the size and location of the lesions, and it is slowly spreading even in Western countries. Even for skilled endoscopists, ESD is a challenging procedure and submucosal fibrosis can be an additional and often unexpected obstacle to technical success

Aims & Methods: This study aimed to assess the outcomes and the safety of ESD as treatment for gastrointestinal lesions with submucosal fibrosis detected during the procedure. All consecutive patients undergoing ESD at our center as first treatment for gastrointestinal lesions were prospectively enrolled from March 2018 to March 2020. Collected data included patient demographics, procedural outcomes and complication rate. Fibrosis was classified as F0 (no fibrosis), F1 (mild fibrosis in the blue submucosal layer), F2 (whitish submucosa or severe fibrosis). According to fibrosis grade, two groups of lesions were defined: no/mild fibrosis (F0-F1) and severe fibrosis (F2).

Results: Overall, 111 patients (65.8% males, median age 70.9 years) with 111 lesions undergoing ESD were enrolled. 78/111 (70.3%) were colorectal lesions, while 33/111 (29.7%) were located in the upper GI tract. Mean lesion size was 36.7 mm (range 15-82 mm).

Technical success rate was 110/111 (99.1%). En bloc resection was not achieved for one lesion with severe fibrosis (F2).

In the colon-rectum, R0-resection rate was 85.5% for lesions with no/mild fibrosis (F0-F1) and 71.4% for lesions with severe fibrosis (F2) (p=0.16). Curative resection rate was significantly higher for F0-F1 lesions compared to F2 lesions (90.9% vs 73.9%, p=0.049). No difference in complication and bleeding rate between the two groups was highlighted.

In the upper GI, R0 resection rate was similar between F0-F1 group and F2 group: 84.6% vs 85.7%, respectively. Curative resection rate was higher in the F0-F1 group (88.5% vs 71.4%), without statistical difference (p=0.26). Overall complication rate was not significantly different between the two groups, but bleeding rate was significantly higher in the F2 group (28.6% vs. 3.8%, p=0.043).

Overall mean procedure time was higher for F2 lesions (130 vs 92.5 minutes), with no statistical difference (p=0.12).

Conclusion: Based on our experience, ESD is feasible and safe for the treatment of gastrointestinal lesions even when fibrosis is detected during the procedure, but detection of severe fibrosis could affect procedural outcomes and increase complication rates. Knowledge of different techniques as saline immersion ESD, tunnelling ESD and traction methods is pivotal to complete the procedure safely.

Disclosure: Nothing to disclose

P1295 WITHDRAWN

P1296

THE SAFETY AND EFFICACY OF ENDOSCOPIC MUCOSAL RESECTION FOR LARGE AND INTERMEDIATE RECTAL POLYPS PERFORMED IN AN IRISH UNIVERSITY AFFILIATED HOSPITAL

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Introduction: Endoscopic mucosal resection (EMR) is now thought to represent a safer alternative to surgical removal of large rectal polyps and is recommended by the European Society of Gastrointestinal Endoscopy for pedunculated polyps and flat/sessile polyps 10mm or more. The presence of malignancy should be assessed for in all lesions, however reliable assessment is difficult; therefore, all polyps for EMR should be excised with the aim of R0 and en-bloc resections. This is associated with lower recurrence rates and allows for precise histological analysis. A perforation rate <0.2% and bleeding in <1% are recommended for all polypectomy's.

Aims & Methods: To determine the safety and efficacy of endoscopic mucosal resection (EMR) for the removal of rectal polyps.

EMR's for rectal polyps from 2011-2018 were identified from our endoscopy database. Demographics, indications, site and size of polyp, en-bloc or piecemeal resection, histological diagnosis, complications and recurrence rates were documented. 179 polyps were < 10mm and excluded from further analysis; 89 were 10-19mm and classed as intermediate and 17 were 20mm or more and classed as large lesions.

Results: 285 rectal EMR's were performed over 87 months, mean age 62.3 years, mean size 9.15mm (range 2-50mm). Histology; 81% (n=233) adenomas, 8% (n=22) high grade dysplasia, 1% (n=3) malignant. En bloc resection was achieved in 86% (n=244). Recurrence occurred in 4% (n=12). 179 polyps were < 10mm and excluded from further analysis. 89 were 10-19mm - intermediate and 17 were >=20mm - large lesions. There was no difference in en bloc resection rates for large and Intermediate lesions, 13/17 (76%) versus 77/89 (86%). R0 resection was infrequently reported for Intermediate, 31/89 (34%) V's 14/17 (82%) large lesions, p=0.0004. Reported R0 resection rates were similar; 22/31 (70%) intermediate and large 9/14 (64%).

Follow up colonoscopy was available in 92 (87%). Larger polyps were more likely to recur, 4/14 (40%) v's 2/78 (2.5%), OR 15, 95% CI 2.5 to 93.9, p=0.003. R0 resections were less likely to recur, 2/28 (7%) versus 4/11 (36%), p=0.03. 7% (n=7) had previously had surgery or EMR for polyps, none of these had recurrences on follow-up colonoscopy. Overall complication rate was 4.7% (n=4); all self-limiting bleeding not requiring transfusion or admission.

Conclusion: EMR is safe and efficacious for resection of large and intermediate rectal polyps. Higher recurrence rates with larger lesions warrants their careful selection and uptake of enhanced EMR techniques, such as pre-cutting EMR.

Disclosure: Nothing to disclose

P1297

SUCCESSFUL BILIARY NAVIGATION USING AIR IN MALIGNANT AND POST-SURGICAL HILAR STRICTURES: A PROSPECTIVE CONTROLLED TRIAL

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Introduction: Patient with biliary obstruction have high risk of cholangitis post ERCP.

Aims & Methods: We aimed to compare the feasibility and results of air versus Urographin in biliary navigation. From May 2016 to May 2017; 80 patients with hilar stricture were enrolled in this study, they were subdivided into 2 groups with equal number; Air and standard Urographin were used as a contrast in both groups respectively, Klatskin tumor was the most common cause of obstruction. Patients were evaluated at day one, day 7 and day 30 after stent placement.

Results: Successful biliary mapping, stent placement and drainage were achieved in all patients. There was no significant difference in age, gender, clinical presentation, liver function tests, and cause of stricture between both groups; ($p > 0.05$). Compared with the use of Urographin, more volume of air and longer operative time were observed. The rate of cholangitis and recovery from cholangitis in air group was significantly less than that in Urographin group (5.6% vs. 33.3%, $p = 0.04$). After ERCP, the mean hospital stay time was shorter in air group compared with control ($p < 0.05$). The difference of 30 days mortality between two groups was significant ($p < 0.05$). The X-ray time was significantly less in Urographin group.

Conclusion: Air was safe, costless and effective in biliary navigation for stent placement in hilar biliary strictures regardless the cause.

Disclosure: Nothing to disclose

P1298

HALF COVERED SELF-EXPANDABLE METAL STENT VERSUS FULLY COVERED AND UNCOVERED SELF-EXPANDABLE METAL STENTS FOR OPTIMIZING BILIARY DRAINAGE IN INOPERABLE DISTAL MALIGNANT BILIARY OBSTRUCTION: A THREE ARMS SINGLE CENTER RANDOMIZED PROSPECTIVE STUDY

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Introduction: Given most patients with distal malignant biliary obstruction (DMBO) present in non-resectable stage, palliative endoscopic biliary drainage with fully covered (FCMS) or uncovered metal stent (UCMS) is the only available measure to improve patients' quality of life. Half covered metal stent (HCMS) has been recently introduced commercially. The adverse effects and stent functioning between FCMS and UCMS have been extensively discussed.

Aims & Methods: We aimed to study the adverse effects and functioning of HCMS versus FCMS and UCMS. Methods: We studied 210 patients and randomized them into three equal groups, HCMS, FCMS and UCMS were inserted endoscopically.

Results: Stent occlusion occurred in (18.6%, 17.1% and 15.7% in HCMS, FCMS and UCMS groups respectively), ($p=0.9$). Stent migration occurred only in patients with FCMS in 8.6% of patients. Cholangitis and cholecysti-

tis occurred in 11.4% and 5.7% respectively in FCMS. Tumor ingrowth occurred only in 10 cases among patients with UCMS after a median of 140 days, sludge occurred in nine, seven and one patients in HCMS, CMS and UCMS respectively, p -value = 0.04).

Conclusion: Given the prolonged stent functioning time, the use of HCMS is preferred than the use of UCMS and FCMS for optimizing biliary drainage in patients with DMBO

Disclosure: Nothing to disclose

P1299

EFFICACY AND SAFETY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN FAMILIAL ADENOMATOUS POLYPOSIS PATIENTS AFTER DUODENECTOMY

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Introduction: Patients with familial adenomatous polyposis (FAP) that develop advanced duodenal polyposis require duodenectomy to prevent malignancy. Pancreatic and biliary complications are common in postsurgical FAP patients. There are no studies evaluating ERCP in FAP patients who have undergone duodenectomy.

Aims & Methods: We seek to report the efficacy and safety of ERCP in FAP patients after duodenectomy. FAP patients who underwent duodenal resection, including pancreas-sparing duodenectomy (PSD) and pancreaticoduodenectomy (PD), from 1992-2019 were identified at a quaternary referral center. Those who underwent ERCP for pancreatic or biliary indications were included. Demographics, technical success, complications, and clinical outcomes were collected from medical records. Technical success was defined by ability to complete the intervention, including intubation of the afferent limb, identification of the pancreatojejunostomy (PJ) anastomosis or biliojejunal anastomosis, and duct cannulation. Complications were defined by perforation, immediate or delayed bleeding, and post-ERCP pancreatitis. Clinical outcomes were defined by rates of technical success, recurrent pancreatitis, and surgical interventions. Continuous variables are presented as median [first interquartile - third interquartile], and mean $\pm$ standard deviation.

Results: Of 110 FAP patients who underwent duodenectomy, 21 ERCPs were performed in 15 patients. 19 were for pancreatic indications (18 pancreatitis, 1 identification of PJ anastomosis), and 2 for biliary indications. The mean age at time of procedure was 59 $\pm$ 11.1 years. 53.3% of patients were male. The median time between duodenectomy and ERCP was 5.6 [2.2, 9.9] years. Of these 15 patients, 12/15 (80%) had pancreas-sparing duodenectomies and 3/15 (20%) had PD. Technical success of ERCP was only achieved in 12/21 (57.1%) ERCPs. The primary cause of failure was the inability to identify the PJ anastomosis in 7/19 (36.8%) ERPs for pancreatic indications. Clinically, 5/9 (55.6%) patients with failed ERP developed future episodes of pancreatitis. Surgery was required in 2/9 (22.2%) patients, and repeat ERP was done in 6/9 (66.7%) patients with failed ERP after duodenectomy. Complications of ERCP occurred in one (4.8%) procedure due to post-ERCP pancreatitis, and there were no perforations or bleeding complications (Table 1).

Conclusion: The technical and clinical success of ERCP in FAP patients after duodenectomy is low. The technical success of ERCP is most commonly due to the inability to identify the PJ anastomosis given the altered

anatomy and jejunal polyposis after duodenectomy. Patients with failed ERP continue to experience recurrent pancreatitis. Procedural innovation and use of advanced techniques, such as endoscopic ultrasound pancreatic duct rendezvous, may be required to manage these patients.

Disclosure: Nothing to disclose

Age at intervention (years)	59 +/- 11.1
Sex: Male	8/15 (53.3%)
Duodenectomy Type: Pancreas-sparing Duodenectomy; Pancreaticoduodenectomy	12/15 (80%); 3/15 (20%)
Median Time from Surgery to ERP (years) [IQR]	5.6 [2.2, 9.9]
Outcomes of ERCP in Post-Duodenectomy FAP patients	No. Patients (%)
Technical Success of ERCP (N=21)	12/21 (57.1)
Technical Success of ERC (N=2)	2/2 (100)
Technical Success of ERP (N=19); Intubation of Afferent Limb; Identification of PJ Anastomosis; Cannulation of PJ Anastomosis; *One ERP did not attempt to identify the PJ anastomosis	10/19 (52.6); 19/19 (100); 11/19 (57.9)*; 9/11 (81.8);
Clinical Outcomes of Patients with Failed ERP (N=9): Recurrent Pancreatitis after Failed ERP; Surgical Intervention; Repeat ERP	5/9 (55.6); 2/9 (22.2); 6/9 (66.7)
Complications of ERCP (N=21): Perforation; Immediate or Delayed Bleeding; Post-ERCP Pancreatitis	0/21 (0); 0/21 (0); 1/21 (4.8)

[Table 1. Characteristics and Outcomes of ERCP in Post-Duodenectomy FAP patients (N=21)]

P1300 WITHDRAWN

P1301

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR BILE DUCT OBSTRUCTION DUE TO METASTATIC BREAST CANCER

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Introduction: More than 2 million new cases of breast cancers are diagnosed every year. Approximately 6% are metastatic at diagnosis in developed countries, while 20-30% eventually develop metastatic breast cancer (MBC). Most common sites of metastases are bone, lung, liver and brain. Reports of biliary obstruction due to MBC are scarce. We summarize 11 MBC cases with bile duct obstruction treated with endoscopic retrograde cholangiopancreatography (ERCP). To the extent of our search, this is largest case series to date on bile duct obstruction due to MBC and the first to focus on ERCP for its treatment.

Aims & Methods: We reviewed records of ERCP procedures at St. Luke's International Hospital performed over the 10 year period from February 1, 2010, to January 31, 2020. Those with a history of breast cancer as indicated on discharge summaries were selected for review. A retrospective electronic chart review was conducted on each selected patient to extract data on demographics, medical history relating to breast cancer, reason for ERCP procedures, clinical variables, adverse events, and outcomes. The key objective was to determine the causes and outcomes of obstructive jaundice in breast cancer patients. In particular, we sought to identify characteristics of bile duct obstruction caused by breast cancer metastases.

Results: 50 ERCP procedures were performed on 35 patients with a history of breast cancer. Indications were of obstructive jaundice were common bile duct stones in 14 patients (40.0%), MBC in 11 patients (31.4%), primary pancreatic ductal adenocarcinoma in 6 patients (17.1%), tumors from other organs in 3 patients (8.6%), and inflammatory stenosis in 1 patient (2.9%).

All 11 MBC cases were women with a median age of 55 (30-66). Bile duct obstruction was seen in all cases, caused by lymph node metastasis in 4 cases (36.4%), pancreatic metastasis in 3 cases (27.3%), liver metastasis in 3 cases (27.3%), and peritoneal carcinomatosis in 1 case (9.1%). 4 cases (36.4%) had duodenal stenosis, which led to ERCP failure in 2 cases (18.2%). Difficult bile duct cannulation was seen in 8 cases (72.7%). Symptomatic complications were seen in 3 cases (27.3%). While clinical success was ultimately achieved in 9 cases (81.8%), median survival after bile duct obstruction was only 2.1 months.

Conclusion: Metastases from breast cancer can obstruct various parts of the biliary tree. ERCP in MBC patients can be difficult and should be approached with caution.

Disclosure: Nothing to disclose

P1302 WITHDRAWN

P1303

DIGITAL CHOLANGIOSCOPY FOR DETECTION OF MISSED STONES IN THE BILE DUCTS AFTER ENDOSCOPIC THERAPY- A SINGLE CENTER STUDY

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Introduction: Occlusion cholangiogram is always performed after conventional endoscopic stone extraction to confirm ductal clearance. Retained stones can be easily missed fluoroscopically and they can be a reason for recurrent biliary symptoms, acute cholangitis, pancreatitis or stone recurrence in the future.

Aims: To evaluate the efficacy and safety of digital cholangioscopy for detection of missed or retained bile ducts stones after conventional endoscopic therapy.

Methods: Data was collected retrospectively from a prospective data base from January to December 2018. For this period a total of 149 patients with choledocholithiasis were treated by ERCP and stone removal. Among them 38 patients underwent digital cholangioscopy after stone extraction and negative occlusion cholangiogram to exclude residual stones. The indications for cholangioscopy were at least one of the following: when mechanical lithotripsy was performed, when multiple stones (over 3) were extracted or when the common bile duct was dilated (over 15 mm), leading to difficulties to obtain good quality cholangiography.

We also explored factors like common bile duct diameter, presence of distal bile duct stricture, duodenal diverticula or surgically altered anatomy and their possible relation with the probability of missed stones.

Results: Residual stones were found in 26,3% (10) of cases. In 18,4% (7) the stones were in the common bile duct, in 5,3% (2) in the intrahepatic bile ducts and in 2,6% (1) in the cystic ducts stump. No correlation between the common bile duct size and the presence of residual stones was found. The distal common bile duct stricture, duodenal diverticulum or surgically altered anatomy were not found to be risk factors for retained lithiasis after conventional endoscopic therapy. No adverse events were observed in the studied group of patients.

Conclusion: Factors like common bile duct size, presence of ductal stricture, duodenal diverticulum or surgically altered anatomy cannot predict the risk of residual stones, missed by occlusion cholangiogram. Digital cholangioscopy is safe and highly effective in the detection of fluoroscopically missed bile duct lithiasis and should be considered to confirm ductal clearance in some clinical scenarios. Further studies are needed to evaluate the cost effectiveness

Disclosure: Nothing to disclose

P1304

A SURVEY-BASED STUDY ASSESSING DUODENOSCOPE REPROCESSING METHODS IN EUROPE

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Introduction: Multiple infection outbreaks caused by contaminated patient-ready duodenoscopes have been reported worldwide. This have led to an increased focus on the reprocessing of duodenoscopes used for endoscopic retrograde cholangiopancreatography (ERCP)

Aims & Methods: We aimed to investigate the use of reprocessing methods at different endoscopy facilities in France, Germany, and UK by sending out an electronic survey to gastroenterologist performing ERCPs. Between February 17, 2020 to March 16, 2020 a total number of 105 gastroenterologists performing ERCPs answered an electronic survey concerning duodenoscope reprocessing methods in France, Germany, and UK. The number of responds were equally distributed amongst the three countries (35 respondents in each country). Data were collected using QuestionPro and analyzed in Microsoft Excel.

Results: Across the three countries, data showed that 33% of all ERCP physicians were unaware of the reprocessing method used at their endoscopy unit. Thirty-five percent (35%) of the ERCP physicians report using high-level disinfection (HLD), and 28% report using double HLD (dHLD). Only 5% of the physicians report that they are using HLD in combination with ethylene oxide (EtO) gas sterilization. When asked about their anticipated contamination rate of the duodenoscopes used for ERCP, the average stated contamination rate was 15% across all countries. Amongst the three countries, UK physicians stated the highest contamination rate of 20%.

Conclusion: This study highlights the need for educating endoscopy staff on all levels about the importance of proper reprocessing to minimize cross-contamination. More than 1 out of 3 ERCP physicians were unaware of the reprocessing method used at their endoscopy unit. Additionally, all three countries state anticipated contamination rates ranging from 12% to 20% on average, which corresponds with findings from previous studies.

Country	Reprocessing method (mean)	Anticipated contamination rate (mean)	Annual ERCP volume (mean)
Germany	HLD: 32% dHLD: 24% HLD + EtO: 12% N/A: 32%	12% ($\pm 3.14\%$)	418 (± 38.09)
France	HLD: 40% dHLD: 37% HLD + EtO: 0% N/A: 23%	13% ($\pm 2.64\%$)	268 (± 33.45)
UK	HLD: 31% dHLD: 23% HLD + EtO: 3% N/A: 43%	20% ($\pm 4.28\%$)	412 (± 36.58)

[Duodenoscope reprocessing methods in Germany, France, and UK.]

Disclosure: Sara Larsen and Lotte Klinten Ockert are both employed by Ambu A/S, Ballerup, Denmark

P1305

SURVEY-BASED ASSESSMENT OF MARKET READINESS FOR SINGLE-USE DUODENOSCOPES IN EUROPE - WILL SINGLE-USE DUODENOSCOPES BE THE FUTURE?

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Introduction: Contaminated patient-ready duodenoscopes used for endoscopic retrograde cholangiopancreatography (ERCP) procedures have caused multiple infection outbreaks worldwide. Due to a complex design, duodenoscopes are difficult to reprocess properly, leading to new innovative single-use duodenoscopes entering the market.

Aims & Methods: The aim of this study was to assess the perception of single-use duodenoscopes and investigate the market readiness for adopting the new single-use technology amongst the three largest markets in Europe. Between February 17, 2020 and March 16, 2020 a total number of 105 gastroenterology physicians performing ERCPs answered an electronic survey about their willingness to convert from reusable duodenoscopes to single-use duodenoscopes. The survey was conducted amongst 35 ERCP physicians in France, Germany, and UK, respectively. Data were collected using QuestionPro and analyzed in Microsoft Excel.

Results: Across France, Germany, and UK, ERCP physicians would on average convert 39% of their conventional ERCP procedures to be performed with single-use duodenoscopes. In the UK, ERCP physicians would on average convert more than half of all their ERCP procedures to be performed with single-use duodenoscopes (52%). Germany and France would on average convert 32% and 33% of the procedures, respectively. Physicians who are currently leasing their duodenoscopes will on average convert 57% of their ERCP procedures from reusable to single-use duodenoscopes. This is a significantly larger share, relative to physicians who owns all duodenoscopes, who on average will convert 37% of all ERCP procedures ($p = 0.029$).

Additionally, physicians who are members of value committees had a significantly higher rate of willingness to convert from reusable to single-use duodenoscopes compared to non-members of value committees (48% vs. 35%, $p = 0.021$). When asked about the most important qualities associated with single-use duodenoscopes, "cost transparency" ranked the highest (23%) followed by "eliminated risk of cross-contamination" (20%) and "availability" (19%).

Conclusion: This study found that there is an interest for adopting the innovative single-use duodenoscopes for ERCP procedures in European countries. Results show that endoscopy units currently leasing duodenoscopes would convert a significantly higher share of ERCP procedures to be performed with single-use duodenoscopes. Physicians who are members of value committees were more inclined to convert more procedures to single-use.

Disclosure: Sara Larsen and Lotte Klinten Ockert are both employed by Ambu A/S, Ballerup, Denmark

P1306

ENDOSCOPIC MANAGEMENT OF «DIFFICULT» BILE DUCT STONE DISEASE

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Introduction: Endoscopic papillosphincterotomy (EPT) followed by stone extraction (SE) is the first-line treatment of patients with bile duct stones. In cases of "difficult" bile stone disease (stone size larger than 15 mm, more than two stones, complicated anatomy), conventional treatment won't be enough. In such cases one of the most effective and safe options for the elimination of bile duct stones is to perform additional large balloon dilation (LBD) of the post endoscopic papillosphincterotomy area (post-EPT area), combined if necessary, with mechanical lithotripsy (ML).

Aims & Methods: Aim: to estimate the possibility of the ML and LBD of the post-EPT area or the combination of these methods in the treatment of «difficult» common bile duct stone disease.

Material and methods: The retrospective single center study of endoscopic management of difficult bile duct stone disease was held at the Pirogov Russian Medical University at the Moscow City Hospital #31 from January 2013 to January 2020.

There were 1356 cases of common bile duct stones including 247 (18,2%) cases of «difficult» bile stone disease. There were less than 3 stones in the 167cases (67,6%). Mean size of the largest stone was 16,9 ±5,5 mm. Mean balloon size used for LBD was 14,21±3,1 mm (10-20 mm).

Results: The general success rate was 93,5% (231). Complete clearance after index procedure was achieved in 224 (90,7%) cases. The general complication rate was 3.2%, mortality rate - 1.6%.

ML was carried out in 23.5% (58) of cases, success after first procedure was gained in 87,9%(51) of cases. The morbidity rate was 6,9%. Complications included 1case of perforation, 3 case of post-ERCP pancreatitis. The mortality rate was 3,5%.

LBD was performed in 49,8% (123) of cases, success rate after index procedure was 92,7% (114). The morbidity rate was 3,3%. Complications after LBD included 2 cases of post-EPT bleeding, 1 case of perforation, 1 case of post-ERCP pancreatitis. The mortality rate was 0,81% (one death).

In cases of LBD failure, it was combined with ML (66, 26,7%). The success rate after index procedure was 89,4% (59). The morbidity rate was 3% (2). Mortality rate - 1,5% (1).

Conclusion: Balloon dilation of the post-ERCP area in «difficult» bile duct stone disease is more effective and less traumatic procedure than ML alone. In cases, when LBD of post-ERCP area is unsuccessful, combination of LBD with ML may help to achieve total common bile duct clearance with comparable morbidity level.

Disclosure: Nothing to disclose

P1307

ENDOSCOPIC INTERVENTIONS FOR TREATMENT OF PANCREATIC ASCITES- SIX-YEAR SINGLE CENTER EXPERIENCE

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Introduction: Pancreatic ascites is a rare but severe complication of pancreatic disease, associated with high mortality. There is no established treatment modality. Medical therapy demonstrates low efficacy and is related with high costs and prolonged hospital stay, surgery is aggressive and with high rate of complications and mortality. Endoscopic therapy is probably the most suitable option with highest success rate and lowest complication rate compared to the other available modalities but the literature data is still scant.

Aims & Methods: Objective: We aimed to retrospectively analyze the data on all patients, admitted in our unit, with clinically significant pancreatic ascites over a six-year period.

Methods: All patients with clinically significant pancreatic ascites for at least 2 weeks, hospitalized in our tertiary referral center were included. All patients had paracentesis performed (diagnostic and/or therapeutic) and ascitic fluid analysis demonstrated high protein-, amylase- and lipase-levels. In all patients endoscopic therapy was attempted and analyzed in terms of technical success, clinical success, complications, ascites resolution and recurrence.

Results: Between 2014 and 2020 19 patients with clinically significant pancreatic ascites were admitted in our unit. 15 of them had chronic pancreatitis. Ascites was a complication of severe acute pancreatitis in the late phase in 2. One patient had pancreatic trauma and one patient developed ascites after surgical biopsy of the pancreas. Endoscopic interventions were technically successful in 18/19 patients. Pancreatic sphincterotomy followed by stenting (using plastic stents) of the main pancreatic duct was performed in 12 patients, pancreatic sphincterotomy alone in one, EUS guided drainage of peripancreatic fluid collection alone in one patient, combination of transpapillary stenting and EUS-guided transmural drainage in 2 patients, combination of EUS-guided transgastric drainage of peripancreatic fluid collection and EUS-guided pancreaticogastrostomy in one patient. Only one patient developed complication- sepsis due to infection of residual fluid collections, resolved with antibiotic therapy. Complete resolution of ascites occurred in all patients after successful endoscopic procedure. No recurrence was detected after a median follow up of 1 year (between 3 months and 4 years). No patient died.

Conclusion: Endoscopic therapy is highly effective and safe in patients with pancreatic ascites. Depending on the clinical scenario, various combinations of different endoscopic modalities improves the outcome without increasing the rate of adverse events.

Disclosure: Nothing to disclose

P1308

MACHINE LEARNING APPROACH IN THE STARK INTERNATIONAL STUDY: GRADIENT BOOSTING OUTPERFORMS LOGISTIC REGRESSION TO PREDICT POST-ERCP PANCREATITIS

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Introduction: Post-Endoscopic Retrograde Cholangiopancreatography (ERCP) pancreatitis (PEP) is ERCP most frequent complication. Predicting PEP risk can be determinant in reducing its incidence and managing patients appropriately, however, studies conducted so far identified single risk factors with standard statistical approaches, with limited accuracy.

Aims & Methods: The aim was to build and evaluate performances of machine learning models to predict PEP probability and identify relevant features.

The "STARK project" is an international, multicenter, prospective cohort study focused on PEP-associated factors. Data were randomly split in training (80%) and test set (20%). Models used to predict PEP probability were: gradient boosting (GB) and logistic regression (LR). On the training set, a 10-split random cross-validation (CV) was applied to optimize parameters to obtain the best mean Area Under the Receiver Operating

Characteristics Curve (AUC of ROC). Afterwards, the model was re-trained on the whole training set with the best parameters and then applied on the test set.

Results: 1,150 patients were included. 70 (6.1%) patients developed PEP. GB model AUC in CV was 0.7 ± 0.076 (95% CI 0.64-0.76), LR model 0.585 ± 0.068 (95% CI 0.53-0.63) (p -value=0.012). AUC in test for GB model was 0.671. Most relevant variables for PEP prediction were: total bilirubin, age, body mass index, procedure time, alcohol units/day, previous sphincterotomy, biliary cannulation attempts and use of Ringer's solution.

Conclusion: This is the first study applying machine learning techniques for PEP prediction, with GB significantly outperforming LR model. Relevant variables were mostly pre-procedural except for procedure time, biliary cannulation attempts and Ringer's solution use.

Disclosure: Nothing to disclose

P1309

PARAMETERS ASSOCIATED WITH SPONTANEOUS PASSAGE OF COMMON BILE DUCT STONES AT INDEX ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

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Introduction: Cholelithiasis can be complicated by common bile duct (CBD) stones in around 15% (1-3). Sometimes CBD stones can pass spontaneously, without the need for surgical or endoscopic retrograde cholangiopancreatography (ERCP) interventions. ERCP is considered a high risk procedure with potential fatal complications.

Aims & Methods: This study aimed to identify parameters associated with spontaneous passage of CBD stones at index ERCP. This was a retrospective, single centre study from December 2016 to January 2019. All ERCP procedures to remove radiologically confirmed (ultrasound, Computed Tomography-scan or Magnetic resonance Cholangiopancreatography) CBD stones were included. Patients with previous ERCP and sphincterotomy were excluded. Data examined included patient demographics, Liver functions test (LFT), stone size, number, and time to ERCP. Additionally, we collected data about stone presence/absence on ERCP cholangiogram at time of the procedure. The resulting data was analysed using IBM SPSS version 26.

Results: 263 ERCP procedures were included in the study. Mean age was 69.5 years (Females 56.7%). 74 patients (28%) spontaneously passed their CBD stone prior to the index ERCP. 189 (72%) were found to have CBD stone on the index ERCP cholangiogram.

We found that patients who spontaneously passed the CBD stone were younger compared to those who did not (Mean age 60 years Vs 73 years respectively, $P < 0.0001$).

Smaller stone size was also significantly associated with spontaneous passage, of the 136 patients where size had been documented mean stone size 5.88 ± 2.6 mm were observed in patients with spontaneous passage (40 patients) vs 9.44 ± 4.6 mm in those who did not (96 patients), $P < 0.0001$. 58.2% (110/189) of patients with confirmed stones on fluoroscopy were found to have more than one stone compared to 41.8% (79/189) had a single stone ($P < 0.0001$), while 71.6% (53/74) of patients with clear CBD on ERCP were found to have single stone compared to 28.4% (21/74) had multiple stones ($P < 0.0001$). Therefore, patients with single CBD stone are likely to pass it spontaneously compared to those with multiple stones. The median interval time between imaging and index ERCP showed no significant difference in patients who passed the CBD spontaneously compared to the patients who did not [Median of 16 days (IQR 10, 46) and 14 days (IQR 8, 36) days respectively ($P=0.569$)].

Amongst the 74 patients who spontaneously passed stones 73% still had abnormal LFT when checked within a week before the procedure and no statistical difference was observed between genders (36 Males vs 38 Females), hence neither parameter was deemed to be related to spontaneous passage of CBD stones.

Conclusion: In this study we identified that age, size and numbers of CBD stone are associated with spontaneous passage at index ERCP. Other parameters like interval time between radiological scan and LFT will require further large scale prospective studies to identify if there is any association.

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Disclosure: Nothing to disclose

P1310

THIOPURINES ARE NOT RISK FACTORS FOR POST-ERC PANCREATITIS IN PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by inflammation and fibrosis of intra- and/or extrahepatic bile ducts leading to strictures and dilatations [1]. PSC occurs mostly in patients with inflammatory bowel disease (IBD) and is often associated with autoimmune hepatitis (AIH). When untreated the disease developed into liver cirrhosis, end-stage liver disease and need of liver transplantation. The disease is also a risk factor for cholangiocarcinoma. In Helsinki University Hospital (HUS), ERC is performed in PSC patients: 1. to confirm the diagnosis and to assess the need of endoscopic treatment, 2. to evaluate individual risk for stratification of disease progression, 3. to exclude biliary dysplasia [2]. Risk of post ERC-pancreatitis (PEP) in PSC patients varies from 1 to 7% [3] Thiopurines, i.e. azathioprine (AZA) and 6-mercaptopurine (6-MP) are immunosuppressants used for the treatment of IBD and AIH, but they are associated with an increased risk of acute pancreatitis [4]. However, the role of thiopurines in the risk of PEP is unknown.

Aims & Methods: This observational retrospective case-control study was aimed at evaluating the impact of thiopurines in the PEP risk of PSC patients.

All baseline, clinical and endoscopic data of 372 PSC patients who underwent 1027 ERC between 2009 and 2018 were collected from the PSC registry at HUS. 186 patients treated with thiopurines (study group, SG) and 186 controls matched at baseline for age, sex, body mass index, physical status grade, medication, ERC duration, difficulty, disease severity among other variables, were compared and propensity score was used for matching. Study group underwent 507 ERCs, whereas control 520 ERCs. Odds ratios (ORs) and 95% confidence interval (95%CI) were calculated as appropriate. Univariate and multivariate logistic regression analysis and generalized linear mixed model (GLMM) were performed. P-value was significant when $p < 0.05$.

Results: Thiopurines treatment was currently in use after 352 out of 507 ERCs (67%) in SG. PEP rate was 5.3% in SG and 4.1% in control group

($p=0.465$). In univariate analysis OR, 95%CI for PEP with thiopurine use was 1.12, 0.17-2.03 ($p=0.710$). In the multivariate analysis, OR, 95%CI for PEP with thiopurine use was 0.99, 0.52-1.88 ($p=0.986$); the factors that seemed to increase the PEP risk were unintentional pancreatic duct (PD) cannulation (OR, 95%CI: 3.04, 1.32-7.02, $p=0.009$), prior PEP (OR, 95%CI: 2.69, 1.28-5.68, $p=0.009$) and periampullary diverticulum (OR, 95%CI: 3.97, 1.45-10.89, $p=0.007$). In GLMM with logistic link statistically significant predictors of PEP were unintentional PD cannulation (OR 3.19, $p=0.002$) and prior PEP (OR 3.3, $p=0.001$).

Conclusion: Thiopurine use did not increase the risk of PEP in PSC patients undergoing ERC. Our result suggests that PSC patients with IBD or AIH can continue thiopurine use when scheduled for ERC.

	Study group (507 ERCs)	Control group (520 ERCs)	p-value
Post ERC pancreatitis, %	27 (5.3)	22 (4.2)	0.465
Inflammatory bowel disease, %	449 (88.6)	460 (88.5)	1.000
Autoimmune hepatitis, %	74 (14.6)	32 (6.2)	<0.001
Rectal diclofenac prior ERC, %	259 (51.1)	245 (47.1)	0.212
Post ERC bleeding, %	4 (0.8)	1 (0.2)	0.212
Post ERC cholangitis, %	7 (1.4)	5 (1.0)	0.574

[Patient and procedure characteristics]

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Disclosure: Nothing to disclose

P1311 WITHDRAWN

P1312

OUTCOMES OF ENDOSCOPIC GALLBLADDER DRAINAGE IN HIGH-RISK PATIENTS WITH ACUTE CHOLECYSTITIS: ENDOSCOPIC GALLBLADDER STENTING VERSUS ENDOSCOPIC ULTRASOUND-GUIDED GALLBLADDER DRAINAGE

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Introduction: Emergent cholecystectomy is recommended for acute cholecystitis (AC). However, cholecystectomy is occasionally difficult in high-risk surgical patients with any comorbidities. Therefore, endoscopic gallbladder drainage is a promising alternative to cholecystostomy. There are two methods for endoscopic gallbladder drainage as follows: endoscopic

gallbladder stenting (EGBS) and endoscopic ultrasound-guided gallbladder drainage (EUS-GBD). However, there are limited data comparing the clinical outcomes of treatment with EGBS and EUS-GBD.

Aims & Methods: This study aims to compare the efficacy and safety of EGBS and EUS-GBD in high-risk surgical patients with AC. We retrospectively reviewed high-risk surgical patients with AC who underwent EGBS or EUS-GBD between April 2012 and February 2020 at two centers. 35 patients (18 men and 17 women; mean age, 82±8years) underwent EGBS, and 10 patients (4 men and 6 women; mean age, 83±8years) underwent EUS-GBD. The primary endpoints were technical and clinical success for both methods of endoscopic gallbladder drainage. The secondary endpoints were the rate of recurrent cholecystitis and adverse events (AEs).

Results: The technical success rates in the EGBS group and the EUS-GBD group were 91% (32/35) and 100% (10/10), respectively ($p = 0.34$). The conversion of EGBS to percutaneous transhepatic gallbladder drainage or EUS-GBD was performed in three patients. The clinical success rates in the EGBS group and the EUS-GBD group were 100% (32/32) and 90% (9/10), respectively ($p = 0.07$). The median stent patency durations in clinically successful cases in the EGBS group and the EUS-GBD group were 597 days (range, 28-2251 days) and 345 days (range, 36-907 days), respectively ($p = 0.377$). The recurrence rate in the EGBS group was 21% (7/32; cholecystitis in 2 cases and cholangitis in 5 cases) with the successful management of these seven cases by endoscopic re-intervention, while the recurrence rate in the EUS-GBD group was 0% (0/9). AEs in the EGBS group and the EUS-GBD group were 11% (4/35; mild pancreatitis in 3 cases and cystic duct injury in 1 case) and 10% (1/10; suffocation due to aspiration), respectively ($p = 0.90$).

Conclusion: Both EGBS and EUS-GBD were useful as permanent drainage in high-risk surgical patients with AC, although there was a tendency that patients treated with EGBS had a higher recurrence rate of cholecystitis than those treated with EUS-GBD.

Disclosure: Nothing to disclose

P1313

STATIN USE AND RISK OF POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) is one of the most feared complications of ERCP. Much attention has been given on the pharmacologic prevention of this serious adverse event. Evidence suggests that statins may exhibit anti-inflammatory properties in the pancreas but studies have conflicting results on its role on the prevention of PEP.

Aims & Methods: This study aims to investigate whether the use of statins has a protective effect against PEP. A comprehensive, computerized literature search from the PubMed Central, Embase, Cochrane Library, and OVID was performed with the following search terms: statins, lipid-lowering drugs, post-ERCP pancreatitis, pancreatitis, PEP, and prevention. Three cohort studies were selected and validated using the Newcastle-Ottawa criteria. Trial results were combined under a random effects model. The Cochrane Review Manager Software version 5.3 was used for all analyses.

Results: Three cohort studies comprising of 4,682 patients were analyzed. In the random effects model, the pooled odds ratio (OR) of PEP occurrence was 0.53; 95% CI (0.26-1.11). The pooled data of the three studies showed

a trend towards a beneficial effect of statin use and decreasing risk of PEP but did not show a protective effect of the statin. Likewise, there was substantial degree of heterogeneity ($I^2=87\%$). Subgroup analysis was done which include two studies on chronic statin use defined as use for more than six months. It showed a pooled OR of PEP recurrence of 0.39; 95% CI (0.28-0.53) using the random effects model, thereby signifying a protective effect of the drug. The subgroup analysis has also resulted to a statistical homogeneity of the trials ($I^2 = 0\%$).

Conclusion: Chronic statin use for more than six months has a protective effect against PEP. This meta-analysis has shown the potential role of statins as prophylactic agents for PEP. However, further prospective randomized studies are recommended to confirm this relationship.

Disclosure: Nothing to disclose

P1314

CLINICAL EFFICACY AND OUTCOMES OF ERCP FOR THE MANAGEMENT OF BILE DUCT LEAKS: A NATIONWIDE COHORT STUDY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) can safely and effectively manage postsurgical or traumatic bile duct leaks (BDLs)¹. Techniques commonly used include sphincterotomy, stenting, or a combination of both^{2,3}. There is a lack of standardized guidelines regarding the effective management of BDLs. Existing data from prior studies is limited and controversial⁴. Our aim was to evaluate the efficacy, complications and clinical outcomes of different ERCP techniques and intervention timing using a nationwide database.

Aims & Methods: We performed a retrospective analysis in the IBM Explorers database⁵ (1999-2019), a pooled, national, de-identified clinical database of over 64 million unique patients from 26 health care networks and 300 hospitals across the United States. Patient populations were identified using SNOMED and ICD codes. ERCP timing after BDL was classified as emergent (< 1 day), urgent (1-3 days) or expectant (>3 days). ERCP technique was classified into sphincterotomy, stent or combination therapy. Adverse events (AEs) were defined as requiring endotracheal intubation, invasive monitoring, transfusion of blood products, TPN, liver abscess, hemodialysis, pneumonia, sepsis, or shock. ERCP failure was defined as the need for salvage biliary surgery or percutaneous biliary drain placement. Chi-squared test was used to analyze relationships between ERCP timing and AEs and; ERCP techniques and AEs/ERCP failure for BDL.

Results: ERCP was performed 550 patients with BDL. 32.7% were emergent, 16.3% were urgent and 50.9% were expectant. Expectant ERCP had a decreased risk of AE compared to emergent and urgent (17% vs 33% vs 33%, $p < 0.001$). Patients with CHF and COPD had an increased risk of AEs after emergent ERCP. Although CAD and CKD patients had a decreased risk of AEs after urgent ERCP, this did not reach statistical significance in post-hoc analysis. Other demographics and chronic diseases did not impact AEs (Table 1). ERCP techniques used were sphincterotomy (23.6%), stent (36.36%) and combination (14.55%). There was no significant difference in the rate of AEs ($p=0.26$) and ERCP failure ($p=0.9$) based on the type of procedure (Figure 1). Additionally, there was no significance between the 3 groups with regards to demographic parameters.

Conclusion: Patients with BDL who had expectant ERCP had a lower risk of AE which although inconsistent with prior studies, still supports the notion that they do not need to be performed emergently or urgently. Combination therapy had a lower incidence of adverse events compared to

sphincterotomy and biliary stent placement however this did not reach statistical significance. All three techniques had similar efficacy with regards to ERCP failure.

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Disclosure: Nothing to disclose

P1315

THE BENEFITS OF ADDING DIGITAL CHOLANGIOSCOPY IN EVALUATING AND TREATMENT OF POST-TRANSPLANT BILIARY COMPLICATIONS

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Introduction: We aim to explore diagnostic, therapeutic benefits and safety profile of Digital Single-Operator Cholangioscopy (DSOC) in patients with biliary complications after liver transplantation (LT) in cases, failed to be managed with ERCP.

Aims & Methods: We performed a single centre prospective study on the role of DSOC in patients with post-LT biliary complications, enrolled in the period 2016 - 2019. Over this period 21 patients with biliary obstruction after orthotopic LT underwent ERCP, in 9 of cases without success. All 9 were further evaluated using DSOC. A technical success of DSOC consisted in visualization of biliary complication (1) and endoscopic treatment (2). The peri-procedural prophylaxis includes 3-5 days systemic wide spectrum antibiotics.

Results: Average patient age was 50.2 years (77.7% male). Six patients (6/9) were diagnosed with anastomotic stricture, two (2/9) with non-anastomotic stricture and one were proven to have biliary cast syndrome. We achieve accurate diagnosis in 8/9 (88.8%) patients, and 7/9 (77.7%) were successfully managed during cholangioscopy.

In 6 cases the strictures were successfully visualized and cannulation under direct visual control were achieved. One patient, thought to have long anastomotic CBD stricture on imaging modalities including ERCP, further evaluated with cholangioscopy was found to have biliary cast syndrome. The latter was successfully washed out during the procedure, and patient demonstrates stable resolution of cholestasis in follow up of one year.

In 2/9 cases we didn't achieve the therapeutic aim - one patient with large size of anastomotic dehiscence and one with multiple non-anastomotic strictures. Adverse events: One patient (1/9) developed mild pancreatitis, completely resolved in three days.

Conclusion: Our study demonstrates DSOC benefits translated into an increase of endoscopic treatment success rate. In our regard, cholangioscopy could spare the need of surgical revision in selected patients. No serious adverse events related to procedure were observed.

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Disclosure: accepted for oral presentation at ESGE and poster at DDW

P1316

IMPACT OF OPTIMAL TIMING OF EARLY PRECUT SPHINCTEROTOMY ON THE RISK OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY RELATED ADVERSE EVENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) has become an invaluable procedure in the diagnosis and management of pancreaticobiliary disorders. Selective cannulation of the common bile duct (CBD) is a prerequisite for successful therapeutic ERCP. Cannulation can be difficult and may fail in 5% to 20% of cases using standard cannulation techniques even when performed by experienced endoscopists. Precut sphincterotomy is a technique used to gain access to the CBD when standard methods have failed. Needle-knife precutting is the most widely used method and has been reported to improve selective biliary cannulation success rates; but, some studies have demonstrated high rates of complications associated with this technique. Recent data confirmed that the impact of precut sphincterotomy depends on timing. Two meta-analyses found that early precut sphincterotomy is associated with lower risk of post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) compared with persistent cannulation attempts. However, the definition of difficult or failed biliary cannulation varies among different studies; hence, comparison between these studies are inappropriate.

Aims & Methods: We conducted this meta-analysis to investigate whether early precut sphincterotomy is associated with increased risk of procedure-related adverse events (PRAE) including pancreatitis, bleeding and perforation in comparison with persistent attempts of biliary cannulation. We also aim to determine the optimal timing of precut sphincterotomy to prevent development of PEP.

A systematic search on four online databases was done, looking for relevant studies reporting on the incidence of PRAE between early precut sphincterotomy group (EPG) and persistent cannulation group (PCG). Nine studies were selected and validated using the Cochrane risk-of-bias assessment tool and 1 study using the Newcastle Ottawa scale. Trial results were analyzed using Cochrane Review Manager software version 5.3, using Mantel-Haenszel method with a random-effects model of analysis. The primary endpoints were the overall incidence of PEP and optimal time for precut sphincterotomy. Secondary outcomes were overall PRAE rate, incidence of bleeding, perforation and overall success rate of biliary cannulation.

Results: Nine RCTs and 1 retrospective cohort (1,571 of 14,017 screened patients) were included in this meta-analysis based on the inclusion criteria. Pooled incidence showed a statistically significant decrease in rates of PEP in EPG with a risk of 4.3% (32 cases of 730 patients) compared with 7.5% (63 cases of 841 patients) risk in the PCG (RR 0.60; 95% CI 0.39-0.92). Using a random effects model, the test for heterogeneity showed an $I^2 = 0\%$ and $Ch^2 = 5.97$. Furthermore, subgroup analysis stratified based on the timing of precut sphincterotomy showed that studies performing precut

sphincterotomy at 5-10 minutes from initial cannulation has significantly lower rates of PEP (RR 0.50; 95% CI 0.26-0.94); while the other subgroups showed insignificant trend towards EPG.

Conclusion: This meta-analysis suggests that compared with persistent biliary cannulation attempts, early precut sphincterotomy was associated with a significantly decreased risk of developing PEP, but are comparable in terms of incidence of bleeding and perforation. In addition, subgroup analysis showed that performing precut sphincterotomy after 5 minutes, but not exceeding 10 minutes of failed biliary cannulation has the further benefit of having 50% less risk of developing PEP.

Disclosure: Nothing to disclose

P1317

PROGNOSTIC FACTORS ASSOCIATED WITH 6-MONTH MORTALITY OF CRITICALLY ILL ELDERLY PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT WITH SEVERE ACUTE CHOLANGITIS

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Introduction: Little is known about the outcomes of elderly patients admitted to the intensive care unit (ICU) with severe acute cholangitis (SAC). The objectives were to describe the 6-month mortality in patients with SAC aged 75 years or over and to identify factors associated with this mortality.

Aims & Methods: Bi-center retrospective French study of critically ill elderly patients with SAC conducted between 2013 and 2017. Demographic and clinical variables of ICU and hospital stays with a 6-month follow-up were analyzed. In both centers, endoscopic retrograde cholangiopancreatography could be performed 24/7.

Results: 85 patients aged 83 [80-89] years were enrolled of whom 60% were men. SAC was mostly due to choledocholithiasis (85%). Mean ICU length of stay was 4.6±4.3 days. Admission SAPS II was 50 [42-70]. The ICU and 6-month mortality rates were 18% and 48% respectively. Multivariate analysis showed that malnutrition (OR=34.5, 95% CI [1.4 to 818]) and a lower ΔSOFA score decrease at H48 (OR by unit 0.73, 95% CI [0.5-0.9]) were associated with higher 6-month mortality.

Conclusion: In their decision-making process, ICU physicians could use these data to estimate the probability of survival of an elderly patient presenting with SAC and to offer time-limited trials of intensive care.

Disclosure: Nothing to disclose

P1318 WITHDRAWN

P1319 WITHDRAWN

P1320

CLINICAL PRACTICE PATTERNS OF INDIRECT PERORAL CHOLANGIOPANCREATOSCOPY: AN INTERNATIONAL SURVEY

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Introduction: Indirect peroral cholangiopancreatography (IPOC) is a relatively new diagnostic and therapeutic tool for biliopancreatic diseases. Little is known about regional differences in its use in daily clinical practice. Therefore we conducted an international survey to evaluate differences in IPOC clinical practice patterns between endoscopists from various countries.

Aims & Methods: An online survey was developed comprising 66 questions on the use of IPOC. Questions were grouped into 4 domains, i.e. experience, equipment and technique, biliary and pancreatic indications. The survey was sent to members of the European Cholangioscopy Group and the German Spyglass user group, and any author who published on IPOC in the past 5 years.

Results: In total, 89 respondents completed the survey, from 23 different countries across Europe (n=21) and the Middle-East (n=2). Twenty-four respondents (27%) performed >100 cholangioscopies lifetime and 5 respondents (5.6%) performed >100 pancreatoscopies lifetime. The majority (n=64 (71.9%)) performed <25 pancreatoscopies lifetime. Eighty-four respondents (94.3%) used the Spyglass DS Direct Visualization system. Prophylactic antibiotics are routinely administered by 65 respondents (73%).

Main indications for cholangioscopy were determination of indeterminate biliary strictures (n=87 (97.8%)) and removal of common bile duct (CBD) or intrahepatic duct stones (n=80 (89.9%)), accounting for an estimated use of 41% (IQR 25-60) and 42% (IQR 20-60), respectively, of all cases undergoing cholangioscopy. Only 12 respondents (14.1%) have an institutional standardized protocol for targeted cholangioscopy-guided biopsy sampling. Twenty-seven respondents (33.8%) use IPOC with lithotripsy as first-line treatment in selected patients with CBD or intrahepatic duct stones.

Electrohydraulic (EHL) or laser lithotripsy (LL) are used by 50 (62.5%) and 18 (22.5%) respondents, respectively, and 12 (15%) use both. Pancreatoscopy is used for removal of pancreatic duct stones, determination of pancreatic duct strictures and delineation of intraductal papillary mucinous neoplasm, by 67 (75.3%), 40 (45%) and 32 (36%) respondents, respectively. Removal of pancreatic duct stones accounts for an estimated use of 72% (IQR 50-95) use of all cases undergoing pancreatoscopy. EHL or LL are used by 46 (68.6%) and 13 (19.4%) respondents, respectively, and 8 (11.9%) use both.

Conclusion: This is the first international survey on the clinical practice of IPOC. There is a wide variation in experience, indications and techniques of IPOC. These results emphasize the need of studies and development of an international consensus guideline to standardize the practice and quality of IPOC.

Disclosure: Nothing to disclose

P1321

QUALITY OF ERCP IN THE NETHERLANDS BASED ON A NATIONWIDE MANDATORY REGISTRATION

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Introduction: In recent years quality assurance in ERCP has gained significant interest and awareness in the Netherlands. Since January 2016 all endoscopists in the Netherlands are obligated to document and register procedural aspects and outcome of all their ERCP procedures in a nationwide quality registry. ERCP procedures are registered either directly into the registry or via a structured reporting tool. In 2014, Ekkelenkamp et al. [1] published the results of a nationwide ERCP registry showing an overall procedural success rate of 86%, but this assessment was based on voluntary registration.

Aims & Methods: This study aims to re-evaluate the quality of ERCP in the Netherlands by analysing the mandatory registry data of centers that use the structured reporting tool. This study was conducted with data from a multicenter database that collects the mandatory ERCP registry data from a structured reporting tool. Endoscopy characteristics and outcomes are automatically extracted from all ERCP reports and stored in the database. Data from between 2017 and 2019 were analyzed. Primary outcome measure was cannulation of the desired duct. Secondary outcome measure was procedural success in relation to the recorded objective of the procedure.

Results: During the 3-year period, 9610 ERCP procedures were performed by 14 centers and recorded in the database, 65 procedures were excluded because the patient age was below 18 years (n=44) or a system error (n=21). A total of 9545 ERCP procedures were included for analysis. In 92.3% of the cases cannulation of the desired duct could be determined, which was successful in 92.3% of patients. In patients with native papillary anatomy it was 89.3%. The objective of the ERCP was documented in 81.6% of the cases in which an overall procedural success rate was achieved of 87.3%.

Conclusion: This is the first study that reports on procedural outcomes of ERCP in the Netherlands since the implementation of a nationwide quality registry. The requirement for mandatory registration allowed for a reliable assessment and demonstrates that the quality of ERCP performed in the Netherlands is high and has improved since quality registration is made obligatory.

References: 1. Ekkelenkamp, V.E., et al., Prospective evaluation of ERCP performance: results of a nationwide quality registry. *Endoscopy*, 2015. 47(6): p. 503-7.

Disclosure: Nothing to disclose

P1322 WITHDRAWN

P1323

ENDOSCOPIC TREATMENT OF BENIGN BILIARY STRICTURES ASSOCIATED WITH ACUTE BILIARY PANCREATITIS

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Introduction: In acute pancreatitis (AP), biliary stricture can develop due to compression of the retropancreatic common bile duct by edematous and inflamed pancreatic tissue. However, there is limited data about its frequency and treatment. In this study, we evaluated the clinical course of patients who underwent endoscopic treatment of benign biliary stricture (BBS) associated with acute biliary pancreatitis (ABP).

Aims & Methods: The study was prospectively conducted in patients with AP who were admitted to a tertiary reference center of Turkey. Patients who had choledocholithiasis and/or signs of biliary obstruction according to the laboratory and imaging methods underwent ERCP. Those with BBS due to inflamed pancreatic tissue constituted the study group. Patients with biliary obstruction due to a pseudocyst or walled-off necrosis, recurrent acute pancreatitis, chronic pancreatitis and a non-biliary etiology were excluded. BBS was defined as distal narrowing of the common bile duct associated with proximal dilatation and delayed drainage of the contrast agent into the duodenum.

Endoscopic treatment was performed by inserting a single 7F or 10F plastic stent, depending on the tightness of the stricture, which was exchanged every 3 months until stricture resolution. Stricture resolution was defined as easy passage of an 8.5mm balloon and rapid emptying of the contrast agent through the stricture. Primary outcomes were to determine the resolution rate of BBS after endoscopic treatment and the time to achieve resolution.

Results: Out of 726 patients with ABP, 257 (35.6 %) underwent ERCP. Among them, 26 (3.6 % of all ABP patients) patients (13 female; mean age: 54.7±18.5 years) had BBS due to inflamed pancreatic tissue and underwent dilation with 7F (n=18 patients) or 10F (n=8) stents. The frequency of BBS was 3.4 %, 5.7 % and 4.8 % in patients with mild, moderate and severe AP, respectively (p>0.05).

There was no significant difference between the frequency of BBS in patients with edematous 3.4 % (23/670) and necrotizing 5.9% (3/51) AP. Long term results of stenting treatment could be evaluated in 21 patients because of mortality due to severe AP and other causes in 1 patient, each and lost to follow up in 3 patients. Stricture resolution could be achieved in all of the patients after endoscopic treatment.

Time to achieve resolution was 3 months in 14 patients (66.7%), 6 months in 5 patients (23.8%) and 9 months in 2 patients (9.5%). The total number of ERCP sessions was 57 (median: 2(1-5)). Stent migration was observed in 4 patients (19 %). None of the patients developed bleeding, perforation or AP. There was no recurrence of BBS during a median follow-up of 28 (12-45) months.

Conclusion: Some of patients with ABP develop stenosis of the intrapancreatic portion of the CBD due to external compression by inflamed and edematous pancreatic tissue. AP-related biliary strictures resolving with time. Biliary stenting is a highly effective and safe method in the treatment of BBS associated with AP until the compression-induced blockage spontaneously resolves.

Disclosure: Nothing to disclose

P1324

EMERGENT VS. URGENT ERCP IN ACUTE CHOLANGITIS: A 20-YEAR NATIONAL POPULATION-BASED ANALYSIS

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Introduction: Acute cholangitis (AC) typically presents with a triad of abdominal pain, fever, and jaundice. Majority of patients require hospitalization, and 20-30% require biliary drainage with ERCP. Recent meta-analyses report early ERCP (< 48 hours) results in lower inpatient mortality, organ failure, and shorter length of stay.

Aims & Methods: We aim to conduct a national population-based analysis to compare timing of ERCP in patients with cholangitis and subsequent outcomes. A population-based study was conducted using a cloud-based database to collect aggregated de-identified electronic health records between 1999 - April 2020. A temporal relationship was established with a first time index event for "cholangitis" with subsequent "ERCP" using SNOMED-CT search criteria.

Our primary outcome was all-cause mortality. Secondary outcomes were findings of disease-related conditions: sepsis, septic shock, bacteremia, and post-ERCP complications. Chi-squared and Fisher-Irwin tests of two-by-two tables were used to generate *P*-values where < 0.05 was considered statistically significant.

	< 24 hrs.	< 48 hrs.	P (< 24 vs. < 48 hrs.)	> 48 hrs.	P (< 48 hrs. vs. >48 hrs)
Male, n (%)	6,890 (41.3)	8,120 (41.0)	0.5604	9,280 (41.5)	0.2981
Female, n (%)	9,930 (58.7)	11,660 (58.9)	0.6980	13,070 (58.5)	0.4052
Age 18-65 yrs.	7,710 (45.6)	9,100 (46.0)	0.4432	10,530 (47.1)	0.0239
Age >65 yrs.	9,060 (53.5)	10,520 (53.2)	0.5658	11,710 (52.4)	0.1006
Race, n (%)					
Caucasian	13,400 (79.2)	15,670 (79.2)	1.000	17,960 (80.3)	0.0050
African American	1,460 (8.6)	1,760 (8.9)	0.3433	2,260 (10.1)	< 0.0001
Asian	390 (2.3)	450 (2.3)	1.000	440 (2.0)	0.0337
Hispanic/Latin American	230 (1.4)	270 (1.4)	1.000	280 (1.3)	0.3741
Insurance type, n (%)					
Private	8,630 (51.0)	9,970 (50.4)	0.2834	11,730 (52.5)	< 0.0001
Medicare	6,360 (37.6)	7,430 (37.5)	0.8525	9,040 (40.4)	< 0.0001
Medicaid	1,900 (11.2)	2,260 (11.4)	0.5726	2,600 (11.6)	0.5207
Related conditions, n (%)					
Sepsis	4,400 (26.0)	5,070 (25.6)	0.3825	6,010 (26.9)	0.0025
Septic shock	870 (5.1)	990 (5.0)	0.6626	1,270 (5.7)	0.0015
Bacteremia	6,010 (35.5)	6,980 (35.3)	0.6896	8,860 (39.6)	< 0.0001
Post-ERCP complications, n (%)					
Pancreatitis	2,530 (15.0)	2,790 (14.1)	0.0222	2,500 (11.2)	< 0.0001
Perforation	100 (0.6)	120 (0.6)	1.000	110 (0.5)	0.1648
Bleeding	280 (1.7)	300 (1.5)	0.1518	300 (1.3)	0.0805
All-cause mortality, n (%)	1,980 (11.7)	2,300 (11.6)	0.7659	3,060 (13.7)	< 0.0001

[Demographical and Disease-Related Complications Comparison in Urgent vs. Emergent ERCP for Cholangitis]

Results: Exploratory database identified 59,070 patients diagnosed with AC who underwent ERCP, of which 16,920 were within 24-hours, 19,790 were within 48-hours, and 22,360 were after 48-hours. All three study arms had similar demographical data (*P* > 0.05) with one exception; patients with ERCP after 48-hours of AC diagnosis were younger (47.1% vs. 46%, *P* = 0.0025). Disease-related conditions were similar in patients with ERCP within 24-hours vs. those with ERCP within 48-hours. Patients with AC with ERCP after 48-hours had worse outcomes with higher rates of sepsis (26.9% vs. 26.0%, *P* = 0.025), septic shock (5.7% vs. 5.0, *P* = 0.0015), bacteremia (39.6% vs. 35.3%, *P* < 0.0001) as well as all-cause mortality (13.7% vs. 11.6%, *P* < 0.0001). Post-ERCP pancreatitis interestingly had higher rate in the <48 hour cohort vs. >48 hour cohort (*P* < 0.0001). Post-ERCP perforation and bleeding had similar rates in all cohorts (*P* > 0.05).

Conclusion: Performing ERCP within 24 vs. 48 hours in patients with acute cholangitis had similar disease-related conditions. Performing emergent ERCP within 48 hours is associated with lower rates of sepsis, septic shock, bacteremia, and all-cause mortality.

Disclosure: Nothing to disclose

P1325

ENDOSCOPIC TRANSPAPILLARY MANAGEMENT OF POSTOPERATIVE PANCREATIC FISTULAS: A TERTIARY CARE CENTER EXPERIENCE

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Introduction: Endoscopic management of postoperative pancreatic fistulas (POPF) has been poorly described. The aim of this study was to describe indications, technique and results of the endoscopic management of POPF.

Aims & Methods: consecutive patients with symptomatic grade B/C POPF receiving endoscopic retrograde cholangiopancreatography (ERCP)-based treatment between 2010 and 2018 were identified from a prospectively maintained database. POPF was classified according to the International Study Group of Pancreatic Fistula. Indications, techniques and results of endoscopic drainage and the patients' outcomes were studied. A logistic regression analysis was carried out to determine predictors of pancreatic fistula closure after endoscopic treatment.

Results: Among 9343 ERCPs performed during the inclusion period, 41 patients had an endoscopically treated POPF (23 women, 18 men, median age ± standard deviation [SD]: 65 years [±14]). Surgeries at the origin of the fistula were: distal pancreatectomy with spleen resection (n=26); spleen-preserving distal pancreatectomy (n=5); central pancreatectomy (n=3); enucleation (n=5); partial pancreatectomy (n=1); left nephrectomy (n=2). At the time of first ERCP, POPF were graded B (n=29) or C (n=12). The median time between surgery and first ERCP was 29 days (SD = 132.4). Eight patients (19.5%) died from surgery-related complications and none from ERCP-related complication. Among the 33 remaining patients, POPF complete resolution rate was 100% within an average of 120.2 days (SD = 79.6)

after the first ERCP, after a median number of 2.0 endoscopic procedure (SD = 1.1). In both univariate and multivariate analysis, older patients, a grade C fistula and an associated sepsis were independent factors of delayed fistula closure or death. No late recurrence of pancreatic leak or collection occurred after the last removal of pancreatic stent.

Conclusion: This retrospective study, the most important reported to date, shows that endoscopic treatment of POPF resistant to medical therapy is an effective option.

Disclosure: Nothing to disclose

P1326

EFFICACY AND SAFETY OF ERCP IN THE VERY ELDERLY WITHOUT PROPOFOL

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Introduction: Efficacy and safety of endoscopic retrograde cholangiopancreatography (ERCP) in elderly patients have been studied extensively but data comparing younger patients with elderly and studies without the use of propofol are scarce. Considering the higher risk of morbidity in the elderly, this data may be important to physicians.

Aims & Methods: The aim of this study was to analyze the patient characteristics and ERCP outcomes between very elderly (age>80 years) and younger patients (age<65 years).

417 consecutive ERCP procedures were performed to 362 patients in our secondary care hospital. Of those, 59 of them (74 sessions) were aged 80 years or older (Group-A) and 173 of them (193 procedures) were aged 65 years or younger (Group-B).

All procedures were performed by the same endoscopist. Endoscopic sphincterotomy (ES) was routinely performed to all naive patients, except there was a contraindication. Endoscopic papillary balloon dilation (EPBD) was routinely performed to all patients with biliary stones. Pancreatic stents used for post-ERCP pancreatitis prophylaxis, in case of unintended pancreatic duct cannulation and septostomy. Biliary plastic stents used for strictures and incomplete clearance of bile duct stones.

All patients were placed in the left semi-prone position, cervical collar applied to help drainage of secretions related to ketamine. Every patient had 2L oxygen via nasal cannula. Rectal indomethacin was administered immediately before the procedure to all patients. Endoscopist-directed deep sedation achieved with intravenous midazolam, ketamine, and pethidine, in combination, adjusted for age and comorbidities. Hyoscine-N-butyl bromide used in all patients for gastrointestinal smooth muscle relaxation. The patients' pulse rate and oxygen saturation were monitored during the procedure with blood pressure measurements every three minutes. Patients were monitored for half an hour in the recovery room and another 24 hours in the medical ward.

ERCP related adverse events were defined as the events which occurred in the day of the procedure and the day after. Early mortality was defined as death within 30 days of the procedure.

Results: The incidence of comorbidities and the use of anticoagulants was increased in Group-A (91% vs 27%, $p < 0.05$ and 52% vs 14%, $p < 0.05$, respectively). ASA levels were higher in Group-A as expected ($p < 0.05$). The number of patients with altered anatomy was also higher in Group-A (11% vs. 0.5%, $p < 0.05$).

The most common indication was common bile duct (CBD) stones in both groups but the incidence was higher in Group-A (66% vs.58%, $p < 0.05$). Gallstone pancreatitis was more frequent in Group-B (25% vs. 11%, $p < 0.05$), stent dysfunction and malignancy were more frequent in Group-A (11% vs 5%, $p < 0.05$ and 5% vs 0.5%, $p < 0.05$ respectively).

The incidence of periampullary diverticula was significantly higher in Group-A (49% vs. 10%, $p < 0.05$) as was the rate of difficult cannulation (27% vs.11%, $p < 0.05$). The number of stones was significantly higher in Group-A (3.4 ± 3.1 vs. 1.5 ± 1.1 , $p < 0.05$). The use of biliary stents was higher in Group-A (18% vs. 6%, $p < 0.05$). The dose of medications used was significantly higher in Group-B ($p < 0.05$). Procedure time was significantly longer in Group-A (34 ± 11.23 vs 26 ± 10.3 , $p < 0.05$). The rate of hypertension was significantly higher in Group-A (n=27, 36% vs. n=30, 60%). The rate of intractable bleeding was also higher in Group-A (n=3, 4% vs. n=2, 1%).

Conclusion: ERCP in the elderly is a safe and effective procedure. Performing ERCP without propofol is well tolerated in these patients.

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Disclosure: Nothing to disclose

P1327

DIGITAL SINGLE-OPERATOR CHOLANGIOSCOPY INTEROBSERVER STUDY USING A NEW CLASSIFICATION: THE MENDOZA CLASSIFICATION

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Introduction: Digital single-operator cholangioscopy (DSOC) allows direct visualization of the biliary tree for evaluation of biliary strictures. However, some criteria from the existing two sets of criteria to evaluate indeterminate biliary strictures: the Monaco criteria and the criteria in Carlos Robles-Medrande's publication (CRM); suffer from poor interobserver agreement (IOA) thus affecting the overall diagnostic accuracy. Our objective was to assess the IOA of DSOC interpretation for indeterminate biliary strictures using a new classification system named the Mendoza criteria.

Aims & Methods: A reference video atlas was created containing video clips and images of 5 criteria based on expert opinion and prior studies. A total of 50 de-identified DSOC video clips were then sent to 14 interventional endoscopists with experience in cholangioscopy. They were asked to score the videos based on the presence following criteria: 1. Presence of Tortuous and dilated vessels, 2. Presence of Irregular nodulations, 3. Presence of Raised intraductal lesion, 4. Presence of Irregular surface with or without ulcerations, 5. Presence of Friability.

The endoscopists then diagnosed the clips as neoplastic or non-neoplastic based on the criteria. Intraclass correlation (ICC) estimates and their 95% confidence intervals were calculated based on a mean-rating (k=14), absolute-agreement, 2-way mixed-effects model.

Results: Clips of 41 malignant lesions and 9 benign lesions were scored. Three out of five revised criteria had almost perfect agreement (range 0.44 to 0.90). ICC was almost perfect agreement for presence of tortuous and dilated vessels (0.86), raised intraductal lesions (0.90), and presence of friability (0.83), substantial agreement for presence of irregular nodulations (0.71), and moderate agreement for presence of irregular surface with or without ulcerations (0.44). The diagnostic ICC was almost perfect agreement for neoplastic diagnosis (0.90) and non-neoplastic (0.90). The overall diagnostic accuracy using revised criteria was 77%, ranging from 64% to 88%.

Conclusion: The IOA and accuracy rate of DSOC using the new Mendoza criteria shows a significant increase of 16% as compared to the Monaco criteria and 20% compared to the Robles criteria. The reference atlas helps with formal training needed to improve diagnostic accuracy.

Disclosure: Michel Kahaleh, Prashant Kedia, Amrita Sethi, Isaac Rajiman are consultants for Boston Scientific

P1328

FIRST INTEROBSERVER AGREEMENT OF OPTICAL COHERENCE TOMOGRAPHY IN THE BILE DUCT: A MULTICENTER COLLABORATIVE STUDY

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Introduction: Optical coherence tomography (OCT) is a technology newly available for evaluation of indeterminate biliary strictures. It allows under-the-surface visualization, theoretically complementing already established modalities such as cytology brushing and cholangioscopy. Preliminary studies have confirmed standardized characteristics associated with malignancy. The aim of this study is to evaluate the first inter-observer agreement in identifying previously agreed upon OCT criteria and making a diagnosis of malignant versus benign disease.

Aims & Methods: A reference video atlas was created containing video clips and images of 8 previously agreed upon criteria based on expert opinion and prior studies. The video atlas was confirmed by expert interventional endoscopists with experience in biliary OCT. A total of 35 video clips were then created. Expert interventional endoscopists scored the video clips for presence of the 8 criteria and for final diagnosis of malignant versus benign. Intraclass correlation (ICC) estimates and their 95% confidence intervals were calculated based on a mean-rating (k=13), absolute-agreement, 2-way mixed-effects model.

Results: A total of 13 interventional endoscopists completed the scoring. Clips of 23 malignant lesions and 12 benign lesions were scored. The ICC using criteria ranged from fair to almost perfect (range 0.3 to 0.86) and (range 0.1 to 0.62) respectively. Almost perfect interobserver agreement was seen with dilated hypo-reflective structures (0.82) and layering effacement (0.86); substantial agreement was seen with hyper-glandular mucosa (0.72), intact layering (0.77), and onion-skin layering (0.77); moderate agreement was seen with scalloping (0.53); and fair agreement was seen with hyper-reflective surface (0.3) and thickened epithelium (2.7). The diagnostic ICC for both neoplastic (0.73) and non-neoplastic (0.75) was substantial interobserver agreement.

The overall diagnostic accuracy was 51%, ranging from 43% to 60%. A majority of interventional endoscopists had performed from 0-10 procedures at the time of the study.

Conclusion: Biliary OCT is a promising new modality for evaluation of indeterminate biliary strictures. After creation of the first video atlas for reference, inter-observer agreement ranged from fair to almost perfect on 8 previously identified criteria. Overall accuracy was fair, though interobserver agreement for malignancy diagnosis was substantial (0.75). Data trends show with more OCT experience, accuracy increases. Further studies after additional endoscopist experience are needed.

Disclosure: Michel Kahaleh, Amy Tyberg and Viren Joshi are Consultants for Ninepoint Medical. Ninepoint Medical funded this study

P1329

SYSTEMATIC REVIEW WITH META-ANALYSIS: ENDOSCOPIC AND SURGICAL RESECTION FOR AMPULLARY LESIONS

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Introduction: Ampullary lesions (ALs) can be treated by endoscopic ampullectomy (EA), surgical ampullectomy (SA) or pancreaticoduodenectomy (PD). However, EA reveals significant risk of incomplete resection while surgical interventions lead to substantial morbidity.

Aims & Methods: We performed a systematic review and meta-analysis to compare R0 resection rate, adverse events (AEs) and recurrence between EA, SA and PD for non-invasive and T1 ampullary tumors. Electronic databases (Medline, EMBASE, SCOPUS) were searched for publications analyzing ALs from 1990 to 2018. R0, AEs and recurrence were calculated as pooled means using a fixed and random-effects model and transformed into a quantity using the Freeman-Tukey Double Arcsine Proportion model. Comparisons were performed by two-sided Student's t-test.

Results: We identified 59 independent studies. The pooled R0 rate was 76.6% (71.8%-81.4%, I²=91.38%) for EA, 96.4% (93.6%-99.2%, I²=37.8%) for SA and 98.9% (98.0%-99.7%, I²=0%) for PD. AEs were 24.7% (19.8%-29.6%, I²=86.4%) for EA, 28.3% (19.0%-37.7%, I²=76.8%) for SA and 44.7% (37.9%-51.4%, I²=0%) for PD. Recurrences were registered in EA in 13.0% (10.2%-15.6%, I²=91.3%), in SA in 9.4% (4.8%-14%, I²=57.3%) and in PD in 14.2% (9.5%-18.9%, I²=0%). Differences between proportions were significant in R0 for EA compared to SA (p=0.007) and PD (p=0.022). AEs were statistically different only between EA and PD (P=0.049) and recurrence showed no significance for EA/SA or EA/PD.

Conclusion: Our data indicate an increased rate of complete resection in surgical interventions accompanied with a higher risk of complications. However, studies showed various sources of bias, limited quality of data and a significant heterogeneity, particularly in EA-studies.

Disclosure: Nothing to disclose

P1330

USE OF ROADMAP FLUOROSCOPY IN UPPER GI ENDOSCOPY

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Introduction: Road Map fluoroscopy (RM) is a radiologic technique that enables visualization of anatomic structures using image subtraction at peak opacification. Our group has reported positive initial experience using RM during interventions.

Aims & Methods: To evaluate the usefulness of RM to guide endoscopic interventions in the esophagus.

Patients and methods: Monocentric observational trial of consecutive patients with upper GI strictures in a university hospital. 38 investigations using RM were performed in 32 patients undergoing endoscopic interventions. Indications for interventions were: balloon dilatation: n= 15 including pneumatic balloon dilatation for the treatment of achalasia, bougienage: n=9 and diagnostic radiography without following intervention: n=1. In addition 14 stents, 7 partially covered and 6 fully covered and one duodenal stent were placed using RM as a guide for exact determination of stent length and diameter. Stents were also deployed under RM guidance.

Results: In all procedures RM successfully guided the intervention. Endoscopic control revealed adequate stent position in all cases. The predicted length of stents by radiological measurements was correct in cases. Later dislocation of stents did not occur.

The resistance during bougienage was matching the location for RM projection of the stenosis. With the help of RM imaging dilatation balloons were easily centered inside the stenosis and thus slipping of the balloon was avoided and not observed.

Adverse events did not occur.

The average radiation dose expressed as dose area product was 86.57 ± 11.8 Gy^m².

Conclusion: As previously reported Road Map fluoroscopy is a safe and simple method for radiographic illustration of stenosis or anatomic changes throughout an endoscopic intervention.

Disclosure: Nothing to disclose

P1331

INTRA-DUCTAL FULLY COVERED SELF-EXPANDING METAL STENTS VERSUS MULTIPLE PLASTIC STENTS FOR TREATING BILIARY ANASTOMOTIC STRICTURES AFTER LIVER TRANSPLANTATION (BASICS)

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Introduction: Fully covered metal stents (FCSEMS) are increasingly used in the treatment of biliary anastomotic strictures (AS) after liver transplantation (LT), as it requires less endoscopic interventions compared to conventional treatment with multiple plastic stents (MPS). However, adverse events such as stent migration and pancreatitis have been reported in previous studies with transpapillary placed FCSEMS.

It is not clear whether this applies to the relatively new intraductal fully covered self-expanding metal stent with a transpapillary extraction string (ID-FCSEMS).

Aims & Methods: The aim of this study was to determine performance of ID-FCSEMS compared to MPS in terms of effectiveness (stricture resolution rate and time to recurrence) and safety for treating AS after LT. Two Dutch LT centers conducted a retrospective analysis of 75 post-transplant patients with AS, confirmed by endoscopic retrograde cholangiopancreatography (ERCP). In Leiden these patients (n=43) were treated with ID-FCSEMS implantation for a period of 6 months. MPS were placed every 3 months over 1 year in patients from Groningen (n=32). Shorter treatment duration was considered in case of early stricture resolution. Stricture resolution was defined as free bile flow across the previous stricture after stent removal, without the need for subsequent dilatation and/or replacement of a stent. Migration was defined as such displacement of a stent that it did no longer crosses the AS.

Results: The stricture resolution rates were high in both groups: 95,3% in ID-FCSEMS and 96,9% in MPS and did not differ significantly (p=1.000). Per patient 2.2 versus 4.2 ERCPs (p=0.000) were performed during an average treatment period of 21.7 versus 24.2 weeks (p=0.574) in the ID-FCSEMS group versus the MPS group. The migration rate of ID-FCSEMS was 14.9%.

Cholangitis occurred less often in patients with an ID-FCSEMS compared to patients with MPS (0.26 vs. 1.1, p=0.005). No other significant differences were observed in adverse events. Stricture recurrence occurred in 25.6% in ID-FCSEMS and 28.1% in MPS (p=1.000). Mean follow up was 42.3 weeks for ID-FCSEMS and 34.2 weeks for MPS.

Conclusion: In the treatment of biliary anastomotic strictures post-liver transplantation the use of intraductal fully covered self-expanding metal stent compared to multiple plastic stents is associated with a similar high stricture resolution rate with less ERCP's and shorter stenting, less cholangitis and otherwise similar safety. Whether optimizing treatment duration improves stricture recurrence warrants further prospective exploration.

Disclosure: Nothing to disclose

P1332

RESCUE GALLBLADDER DRAINAGE FOR NON-CHOLECYSTITIS CAUSES

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Introduction: Endoscopic transpapillary gallbladder (GB) drainage (ETGD) appears to be an effective and safe procedure for patients with symptomatic GB disease who are at high risk for cholecystectomy. In cases other than acute cholecystitis, it may be necessary in ERCP procedures, especially when the use of a fully covered self-expanding metal stents (FC-SEMS) is indicated (rescue gallbladder drainage, RGD). The aim of this study is to share our RGD experience.

Aims & Methods: We retrospectively studied 70 patients who underwent ETGD between 2015-2020. Of 70 patients, 58 (36 F, age: 66.1 ± 19.0 years) underwent ETGD due to symptomatic GB disease and in the remaining 12 (7 M, age: 51.7 ± 20 years) patients ETGD procedure was performed with various indications other than cholecystitis (RGD group). If the FC-SEMS exceeds the orifice of the cystic duct, a 7 Fr double pigtail plastic stent was inserted into the gallbladder. FC-SEMS and plastic stent were removed after 1-3 months. The main clinical features of these patient groups were compared and detailed information was given about the RGD group.

Results: RGD group patients were younger than those with acute cholecystitis group (p: 0.04). Technical success was observed in 55 of 58 (94.8%) patients with cholecystitis and 11 of 12 (91.7%) patients without cholecystitis (p: 0.67).

Eleven patients had stenosis in the distal bile duct (3 portal cholangiopathy, 3 chronic pancreatitis (CP), 1 primary sclerosing cholangitis (PSC), 1 papillary tumour, 1 hemorrhagic pancreatitis, 2 unknown cause), 8 of which had stones in the proximal biliary tract. In an ERCP-related perforation case RGD was performed because FC-SEMS was inserted for peripapillary perforation treatment. The GB could not be cannulated in 1 patient with chronic pancreatitis (technical success rate was 91.7% (11/12). In this patient, stenosis was treated with a plastic stents. In patients with tumors, ERCP perforation and hemorrhagic pancreatitis, stents were kept for 1 to 3 months until surgery (Whipple and cholecystectomy). Stents were removed after 2-3 months in patients with portal cholangiopathy, CP and other two strictures. Stones could be removed in 1-5 sessions. The stones of the patient with PSC could not be removed. This patient was given to surgery. The clinical success rate was 83.3% (10/12). Cholecystitis due to FC-SEMS insertion was not observed in any patients.

Conclusion: Our study shows that, in certain indications, transpapillary gallbladder drainage can be performed as a rescue therapy with high technical and clinical success rate.

Disclosure: Nothing to disclose

P1333 WITHDRAWN

P1334

POST-ERCP PANCREATITIS: PROSPECTIVE EVALUATION OF PREDICTIVE RISK MODELS

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Introduction: Pancreatitis is the main complication of endoscopic retrograde cholangiopancreatography (ERCP). Even though numerous studies have addressed factors that may increase the risk of post-ERCP pancreatitis (PEP), it is not clearly established which combination of these factors classifies procedures as high or low risk. There are several scores designed to identify high risk ERCP. However, these models were never compared and their relative ability to predict PEP is unknown.

Aims & Methods: The aim of this study is to evaluate different PEP risk models in patients submitted to ERCP in a tertiary hospital. ERCP performed between February 2019 and February 2020 were prospectively enrolled. Six scores were identified through a literature review. These scores include patient characteristics as well as endoscopist aspects and technical features. Their predictive ability was assessed through calculation of ROC curve and compared with DeLong test.

Results: A total of 170 ERCP in 143 patients (median age 73 years; 56,5% female) were included. Twelve (7,1%) patients developed PEP. The *Friedland* score presented the best predictive ability with an AUC 0,907 (p<0,001). The *Fujita* score had a fair performance with an AUC 0,728 (p=0,009) for PEP. On the other hand, the *Kamal* score showed an inferior ability to predict PEP (AUC 0,678; p=0,040) and the remaining scores - *DiMagno*, *Putignano* and *Jeurnink* - did not prove useful to predict PEP (p>0,05) in our population.

Conclusion: The *Friedland* score showed an excellent performance in identifying patients at high risk for PEP. Its use in clinical practice might be useful in selecting patients who may benefit from early prophylactic measures.

Disclosure: Nothing to disclose

P1335

INCIDENCE OF POST-ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY PANCREATITIS (PEP) ACCORDING TO THE PROTOCOL OF PROPHYLAXIS USED. A RETROSPECTIVE, CROSS-SECTIONAL OBSERVATIONAL STUDY

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Introduction: Rectal indomethacin or diclofenac, intravenous administration of lactated ringer (LR) and pancreatic duct stenting are recommended measures to prevent PEP

Aims & Methods:

Aim of the study was to compare different protocols of PEP prophylaxis.

Methods: A retrospective, observational and cross-sectional study was conducted. Patients undergoing ERCP for biliary diseases between 2013 and 2019 were included. Patients diagnosed with any pancreatic disease (pancreatic cancer, chronic pancreatitis, previous acute pancreatitis) and post-surgical altered bilio-pancreatic anatomy were excluded. Patients were divided in four cohorts depending on the type of PEP prophylaxis used in different periods. Group I: rectal diclofenac 100mg in high-risk patients of PEP; group II: rectal diclofenac + LR 500 mL in high-risk patients of PEP; group III: rectal diclofenac + LR 500 mL in every patient undergoing ERCP; group IV rectal indomethacin + LR 500 mL in every patient undergoing ERCP. All patients were monitored for pain and serum pancreatic enzymes over 24h after ERCP. Incidence of PEP was calculated and compared by ANOVA. Risk factors for PEP were analysed by logistic regression.

Results: 1,621 patients were included, mean age 71 ± 15 years, 832 males, 455 in group I, 254 in group II, 728 in group III and 184 in group IV. The global incidence of PEP was 3.86% (group I: 2.42%, group II: 3.94%, group III: 4.3% and group IV: 4.9%, p=0.3). Smoking (OR 9.0 CI 95% 1.9-42.1) and cannulation of the pancreatic duct (OR 9.1 CI 95% 1.8-46.0) were the most relevant risk factors for PEP in the era of routine prophylaxis.

Conclusion: This study showed that any combination of either rectal indomethacin or diclofenac with hydration with LR in high-risk patients or in every patient undergoing ERCP are equally effective in preventing PEP. Smoking and cannulation of the pancreatic duct are risk factors of PEP in the era of routine prophylaxis.

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OUTCOMES AND USE OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN HIGH-VOLUME CENTERS - RESULTS FROM DATA OF THE HUNGARIAN ERCP REGISTRY

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Introduction: Patient registries are essential tools to monitor healthcare quality and ensure guideline adherence. The Hungarian ERCP Registry was developed to monitor key performance indicators and quality of service.

Aims & Methods: We aimed to compare our performance to international standards to discover where improvements have to be made. The Hungarian ERCP Registry database was used to analyze data from 7 high-volume centers. Main performance indicators, adverse events, prophylactic measures, difficulty of ERCP were analyzed.

Results: 3260 ERCP procedures were done, from that 1909 ERCPs (58.6%) were carried out on native papilla patients. Biliary cannulation was successful in 92.6% (2943/3179) of all cases with biliary indication while 91.3% (1710/1872) in native papilla cases. The cannulation success rate reduced to 88.1% (897/1018) in difficult biliary cannulation cases. A significantly higher rate of unsuccessful cannulation was seen in grade 4 ERCPs (35.5%).

Post-ERCP pancreatitis (PEP) rate of native papilla cases was 2.5% (48/1909) which was only minimally higher in difficult cannulation cases (3.1%, 32/1045). Most of the PEP cases were mild (71.7%). PEP developed in 8 (16.7% cases after multiple pancreatic guidewire cannulation without prophylactic pancreatic stent (PPS) placement, while only 1 mild PEP developed where neither indomethacin nor PPS were used.

Most quality indicators were met; however, perforations (0.9%) and bleeding complications rate (1.1%) were higher than the expected target. 30-day follow up was only successful in 71.6% of cases, which should be improved to detect delayed adverse events. There was a high variability in the use of indomethacin suppositories among centers (1.7-91.7% of cases).

In one center PEP rate was unexpectedly high (20.4%) in native papilla cases with low number of registered procedures. The rate of successful cannulation in native papilla cases were 1-2% below the 90% threshold only in 2 centers.

Conclusion: Most of the performance indicators of ERCP were met in our high-volume centers, however, there was a considerable deviation from guidelines in PEP prophylactic measures in some centers. Follow-up rate was below the target which should be increased to detect possible late adverse events.

Disclosure: Nothing to disclose

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ANALYSIS OF POST-ERCP PANCREATITIS RATES IN THE HUNGARIAN ERCP REGISTRY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most frequently applied advanced endoscopic technique for therapeutic purposes. However, it comes with a significant risk of adverse events. We aimed to analyse the post-ERCP pancreatitis rates in the Hungarian ERCP registry.

Aims & Methods: Post-ERCP pancreatitis (PEP) rates and prophylactic measures were analysed in the registry data. Until 15th of October 2019 we enrolled 3364 patients in the ERCP registry. From these patients 2706 cases were validated, 1596 were native papilla cases.

Results: PEP occurred in 41 cases (1.5%) if all cases are considered, 2.3% (37/1596) in native papilla cases. PEP prophylaxis (indomethacin (IND) suppositories or prophylactic pancreatic stents (PPS)) were not applied in 35.5% (566/1596) of the cases. PEP developed in 2.3% (13/566) of patient without prophylaxis, 38.5% of these PEP cases were moderately severe (n=4) and severe (n=1). IND alone was administered in 53.3% of the cases (851/1596), the PEP rate was 2.5% (21/851) in these patients. PPS alone was inserted in 4.3% of the cases (68/1596), only 1 patient developed PEP (1.5%, 1/68). Both PPS and IND were applied in 111/1596 cases, 2 patients (1.8%, 2/111) developed PEP. In 186 patients with multiple pancreatic cannulation, PPS was inserted only in 93 (50%). PEP developed in 5 cases (5.4%), 3 of them were moderately severe or severe.

Conclusion: While the average rate of PEP is low in our registry, prophylactic measures are underutilized. Potentially preventable PEP cases were identified in our analysis, and high ratio of these patients developed moderately severe and severe PEP.

Disclosure: Nothing to disclose

P1338

USING DOUBLE WIRE-GUIDED TECHNIQUE WITH TRANSPANCREATIC PAPILLARY SEPTOTOMY IN DIFFICULT BILIARY CANNULATION IN ERCP

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Introduction: Common bile duct (CBD) cannulation can be difficult in up to 10% of ERCPs performed by experienced endoscopists. This situation leads to increased incidence of both unsuccessful procedures and post-ERCP pancreatitis. We report our outcomes using the double wire-guided technique with transpancreatic papillary septotomy in accessing difficult biliary ducts and the complication rates associated with this technique.

Aims & Methods: In our institution, a tertiary care centre, 1440 patients underwent ERCP from January 2017 to December 2019. Clinical charts were reviewed retrospectively. During ERCP, the double wire-guided technique with transpancreatic papillary septotomy was usually attempted if the guidewire has inadvertently been placed on the pancreatic duct for at least two times or immediately after the first pancreatic cannulation, if the overall procedure was taking longer than 10 minutes. Patients requiring this technique were identified and assessed for successful cannulation of the CBD. The use of post ERCP pancreatitis prophylaxis [Pancreatic duct (PD) stenting and/or nonsteroidal anti-inflammatory drugs (NSAIDs)] were also revised. Finally, the incidence of post-ERCP pancreatitis was calculated.

Results: The double wire-guided technique with transpancreatic papillary septotomy was used in 55 patients (30 were males; mean age of 67.9 years). Indications included: biliary stenosis secondary to neoplastic disease of the pancreas (58%, N=32 patients), choledocholithiasis (38.5%, N=21) and bile leak (3.5%, N=2). CBD cannulation was achieved in 49/55 patients (89.1%). In three of the remaining patients, CBD cannulation was achieved using the needle knife precut technique. In the other three the procedure was postponed.

All patients were given a protocol of Ringer Lactate peri-procedure. Post ERCP pancreatitis prophylaxis using PD stenting or NSAIDs suppositories were used in 52/55 (94.5%) and 46/55 (83.6%) patients respectively. The latter was only not administered in case of contraindication, especially kidney lesion. A total of 44 patients (80%) received a triple prophylaxis. Post-ERCP pancreatitis occurred in 5 patients (9%), and of these all received triple prophylactic therapy with Ringer Lactate, PD stent and NSAIDs.

Pancreatitis was mild in all cases with no procedure-related deaths.

Conclusion: The use of the double-wire technique with transpancreatic papillary septotomy is effective in achieving difficult biliary cannulation and does not appear to increase the risk of post-ERCP pancreatitis

Disclosure: Nothing to disclose

P1339

IS TIME TO ERCP A RISK FACTOR FOR THE DEVELOPMENT OF POST-ERCP PANCREATITIS IN NON-ERCP EMERGENCIES PATIENTS?

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Introduction: Early ERCP with biliary drainage is known to improve the outcome in acute cholangitis, still the most favorable time to perform ERCP in obstructive jaundice is not standardized. The aim of this study was to assess if time to ERCP (TtE) is a risk factor for post-ERCP pancreatitis (PEP) or if TtE is influencing hospitalization days in patients without acute cholangitis.

Aims & Methods: We analyzed patients that undergone ERCP during a period of 12 months in our Gastroenterology department. The TtE (meaning the time from admission to ERCP procedure) was quantified per each patient and analyzed if the TtE influenced the PEP development or the patient hospitalization time in patients without acute cholangitis. We exclude from our study patients with acute cholangitis and those with previous ERCP.

Results: From 417 ERCPs performed in one year in our department 60% (251/417) were included in the final study, mean age 65 ± 16 years and 41.8% (105/251) were male. More than a half (67.3%) had benign causes of biliary obstruction. Overall incidence of PEP was 6.8% (17/251). 43% (108/251) of the patients had TtE at 24 h, out of which 5.5% (6/108) developed PEP. TtE within 24-72 h were 37.5% (94/251) patients, out of which 6.4% (6/94) developed PEP. TtE more >72h were 16.7% (42/251) out of which 12% (5/42) developed PEP. Odds ratio for performing ERCP after 24 h showed increased risk of developing PEP, OR=1.5, 95% CI (0.53-4.18) $p=0.447$. If we take a cut off value for hospitalization of 3 days, there was a significant difference between groups according to TtE, 26% (28/108) (ERCP < 24h) had >3 days of hospitalization vs. 84% (114/136) (ERCP>24h, $p<0.0001$). Delaying time to ERCP leads to a prolonged time of hospitalization days with an OR=14.8, 95% CI (7.9-27), $p<0.0001$. The etiology of obstruction did not influenced the risk of PEP, 58.8% of cases had a benign cause of obstruction and 41.2% had a malignant cause $p=0.3120$.

Conclusion: TtE after 24 h had an unremarkable odds ratio when looking at the risk of developing PEP but the hospitalization days were statistically significant if we delay TtE for more than 24h. The etiology of obstruction did not influence the PEP.

Disclosure: Nothing to disclose

P1340

IS ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)-OBTAINED BILE CULTURE WORTH DOING? MICROBIOLOGICAL ANALYSIS OF COLLECTED BILE SPECIMENS AND CLINICAL CONSEQUENCES

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Introduction: Cholangitis in the setting of a malignant or benign stricture or a choledocholithiasis is a common indication for performing an ERCP. Collecting bile specimen during an ERCP is theoretically essential to identify the pathogenic bacteria responsible for the bile tract infection and guide a clinical decision, considering that usually bacteria do not grow in blood cultures in this setting.

Aims & Methods: Our aim was to identify the pathogens growing in bile and blood cultures in an acute cholangitis and evaluate how often the empiric antibiotic treatment had to be changed as well as the clinical outcome of the bile culture-guided antibiotic treatment. Retrospectively we analysed all consecutive patients that underwent biliary drainage for acute cholangitis in our department of endoscopy.

Results: From January 2017 to December 2019, 1.538 ERCP (791 females, mean age of $68,1 \pm 15,7$ years) with a biliary indication were performed in our department of endoscopy. Indications included 708 choledocholithiasis, 356 malignant strictures, 127 benign strictures, 39 bile leaks and 308 other indications. Bile was collected from 412 patients with cholangitis (26,8%). The bile cultures came up positive in 357 cases (86,7%). In 30,5% of the bile cultures grew one microorganism, whereas a polymicrobial growth (two to six microorganisms) appeared to the remaining cultures. Out of totally 819 isolated microorganisms in the bile cultures, the most common were Enterococci (62,7%), Candida (33,9%), Escherichia coli (31,1%), Klebsiella (18,2%), Streptococci (16%), Staphylococci (14%), Enterobacter cloacae (9,8%) and Pseudomonas aeruginosa (7,6%). 160 bacteria demonstrated an antibiotic resistance, of which 39 (24,4%) Vancomycin-resistant Enterococci, 1 (0,6%) Methicillin-resistant Staphylococcus aureus, 45 (28,1%) Enterococci susceptible to glycopeptides, 22 (13,8%) Gram negative bacteria resistant to penicillins and cephalosporines and 20 (12,5%) multidrug resistant gram negative bacteria. According to the obtained bile culture, empiric antibiotic treatment had to be changed in 92 cases (22,3%) with a clinical response in 71 of 92 patients (77,2%). Blood cultures were obtained in 198 of 412 patients (48,1%), whose bile was also collected. In the 69 (34,8%) positive blood cultures, most common pathogens were Escherichia coli (42%), Enterococci (17,4%), Enterobacter cloacae (8,7%), Klebsiella (7,2%), Pseudomonas aeruginosa (4,3%) and Streptococci (4,3%).

Conclusion: In almost a quarter of patients with cholangitis (22,3%) empiric antibiotic treatment had to be changed according to antibiotic susceptibility proven from bile cultures. Our study showed that ERCP-obtained bile culture is even more than blood culture an effective measure in terms of clinical improvement to steer antibiotic treatment, especially in patients with problematic susceptibility to antibiotics.

Disclosure: Nothing to disclose

P1341

ROLE OF ENDOSCOPIC TREATMENT IN MANAGEMENT OF BILIARY COMPLICATIONS OF HEPATIC HYDATID CYST

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Introduction: Tunisia is considered an endemic country of hydatid disease. The liver is most commonly affected and intrabiliary rupture of the cyst is its most serious complication. In clinical practice, endoscopic retrograde cholangiopancreatography (ERCP) is indicated in preoperative frank intrabiliary rupture or for biliary adverse events after surgery.

Aims & Methods: The aim of our study is to assess the role of ERCP in the management of hepatic hydatid disease.

We conducted a retrospective study over a period of 13 years: between January 2006 and December 2019. All patients who had had ERCP for a biliary complication of hepatic hydatid cyst were included.

Results: During the study period, intrabiliary rupture of the cyst represented 6 % (73/1197) of all indications for ERCP. The average age of the patients was 56 years (19-90 years) with a male predominance in 59% of cases (n = 43). The indications for ERCP were: Preoperative in eight patients (11%) for acute cholangitis by opening hydatid cyst in main bile duct (MBD), postoperative in 65 patients (89%) after an average delay of 26 days.

The indications after surgery were: persistent external biliary fistulae in 42% of cases, angiocholitic syndrome in 27% of cases and obstructive jaundice in 31% of cases. MBD catheterization and endoscopic sphincterotomy were successfully performed in 97% (n = 71). ERCP made it possible to objectify a cysto-biliary fistulae in 32% of cases (n = 23), a hydatid material in MBD in 38% of cases (n = 28) and a cholelithiasis in 21% of cases (n = 15). In patients with biliary fistulae, endoscopic sphincterotomy has led to the reversal of bile flow with disappearance of jaundice after an average of 8 days and a drying up of the external bile fistulae after an average of 10 days. No complications related to endoscopic treatment were noted.

Conclusion: In our series, therapeutic ERCP is indicated for postoperative biliary complication in 9/10 of cases. It constitutes an effective treatment with low morbidity.

Disclosure: Nothing to disclose

P1342

THE USE OF SUCTION DURING ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY OF SOLID PANCREATIC LESIONS USING FRANSEEN-TIP NEEDLE: A RANDOMIZED CROSSOVER TRIAL

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Introduction: New endoscopic ultrasound fine-needle biopsy (EUS-FNB) needles with innovative tip geometry (opposing bevel design) have been recently introduced. Franseen design has a tip with three symmetric beveled cutting edges designed to get deep into the tissue and obtain ample tissue volume due to its large crown-tip area. Previous studies with EUS-Fine-needle aspiration (FNA) showed that standard suction increases the

rate of diagnostic samples and sample cellularity. However, suction often results in increased specimen bloodiness, which can affect interpretation. The utility of suction during EUS-FNB using Franseen-tip needle remains unclear and has not been evaluated in randomized trials.

Aims & Methods: We designed a randomized crossover trial to compare the diagnostic yield and quality of tissue specimen during EUS-FNB using a 22G Franseen-tip needle, with and without standard syringe suction. Consecutive patients attending for EUS-guided sampling of solid pancreatic lesions were recruited. A minimum of two passes were performed for each case: one with 20mL syringe suction (S+) and another without the use of suction (S-). The order of passes was randomized (order A: S+/S-; order B: S-/S+) and the pathologist blinded.

Results: A total of 38 consecutive patients were enrolled over a 9-month period. The mean age of the subjects was 65.4±11.0 years; 57.9% (n=22) were male. Lesions were located in the head (n=21, 55.3%), body (n=15, 19.5%), and pancreatic tail (n=2; 5.3%). The overall diagnostic accuracy was 78.9% (30/38 cases). There was no difference between S+ and S- samples, when one of these samples was chosen as the 'most informative' by the pathologist (S+: n=17, 44.7%; S-: n=15, 39.5%; no differences, n=6, 15.8%, p=0.57). A diagnosis of malignancy was obtained in 56 samples/bottles: 28 in the S+ group and 27 in the S- group. Comparing the two groups (S+ vs. S-), the sensitivity, specificity, negative likelihood ratio, positive likelihood ratio, and diagnostic accuracy were 80.0% vs. 77.1%, 100% vs. 100%, 0.20 vs. 0.23, NA in both, and 81.6% vs. 78.9%.

Comparing the two sampling techniques regarding the degree of blood contamination, we found a statistically significant difference between the groups (S+: n=24, 63.2%; S-: n=14, 36.8%, p< 0.01). However, in the sub-analysis of the impact of bloodiness in the ability to provide a histological diagnosis, a negative impact was evident only in samples where no suction was used (S+: OR 1.21, CI95% 0.30-4.87, p=0.78 vs. S-: OR 0.19; CI95% 0.04-0.85, p=0.03).

Conclusion: The use of suction did not impact the diagnostic yield of EUS-FNB using a Franseen-tip needle. but was associated with a higher degree of sample blood contamination that had no effect on the diagnostic performance.

Disclosure: Nothing to disclose

P1343

LAPAROSCOPIC OR EUS-GUIDED GASTROENTEROSTOMY FOR GASTRIC OUTLET OBSTRUCTION: A PROPENSITY SCORE MATCHED ANALYSIS

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Introduction: Gastric outlet obstruction (GOO) is not uncommon amongst patients with gastrointestinal malignancies. Where enteral stenting or laparoscopic gastroenterostomy (LGE) have been advocated in the past, recent evidence suggests that EUS-guided gastroenterostomy (EUS-GE) may provide a safer approach to LGE without sacrificing efficacy. The available comparative studies are mainly of retrospective design, include low numbers of EUS-GE procedures, compare EUS-GE with conventional or open surgical gastroenterostomy and do not correct for selection bias.

Aims & Methods: Our aim was to perform a propensity score-matched analysis of our experience using EUS-GE or LGE for either benign or malignant GOO. A retrospective analysis was performed of all consecutive LGE and EUS-GE procedures performed for gastric outlet syndrome between

January 2015 and April 2020. A propensity score-matched design was used in order to minimize selection bias. Age, sex, underlying disease, disease stage, presence of ascites and/or peritoneal carcinomatosis were used as variables, with a standard maximum propensity score difference of 0.1. All EUS-GE were performed under general anesthesia, using an electrocautery-enhanced lumen apposing metal stent and 'free-hand' technique.

Results: In total, 54 patients were identified, of which 34 patients (63%) were treated with EUS-GE and 20 patients with LGE (37%). The majority of LGE performed in our center were not eligible for inclusion, as they included many adjunctive treatments, such as cholecystectomy, hepaticojejunostomy or for example metastasectomy. Only isolated laparoscopic gastroenterostomies were included. By means of propensity score matching, 11 patients were allocated to both groups, resulting in a total of 22 (1:1) matched patients (median age 59 (IQR 53-69), 50% female, 18% pancreatic cancer, 23% benign disease, 9.1% peritoneal carcinomatosis). Technical success was achieved in 10 out of 11 EUS-GE patients (90.9%) vs. 100% in the LGE group ($p=1.000$). Clinical success, defined as eating without vomiting, was achieved in 100% in both groups. In the EUS-GE group, mean procedure time (55 vs. 105min, $p=0.002$) and mean time to oral intake (0.9 vs. 5.6 days, $p=0.006$) were significantly shorter compared to the LGE group. Using the ASGE lexicon for adverse events (AE), the total number of AE was similar in both groups (1 vs. 5 event(s), $p=0.149$), although moderate and severe events were detected significantly more frequent amongst patients treated with LGE (0 vs. 5 events, $p=0.035$). Evolution in body mass after two months (-1.5 vs. -3.2kg, $p=0.332$) and mean hospital stay (10.1 vs 14.5 days, $p=0.211$) did not differ.

Conclusion: For patients with gastric outlet syndrome, EUS-GE and LGE showed almost identical technical and clinical success, as well as similar effects on hospital stay and body mass. However, shorter mean procedure time, reduced time to oral intake and a lower rate of moderate and severe events were seen in patients treated with EUS-GE. These findings are of great importance in a patient population which is already plagued by reduced quality of life and limited life expectancy.

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P1344

DIRECT ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY WITH LUMEN-APPPOSING METAL STENTS: A RETROSPECTIVE BICENTER STUDY ON TECHNICAL FEASIBILITY AND CLINICAL OUTCOME

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Introduction: Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) with lumen apposing metal stents (LAMS) appears to be a promising intervention in the management of gastroduodenal obstruction as a less invasive alternative to surgery.

Aims & Methods: The aim of this study was to evaluate the feasibility, safety and clinical outcome of direct EUS-GE in patients of surgical high-risk or in a palliative setting. This retrospective bicenter study included

patients who underwent direct EUS-GE with LAMS (April 2017 to May 2020) investigating feasibility, technical success (correctly placed LAMS), clinical outcome (successful oral nutrition) and procedure-associated complications. Direct EUS-GE was performed using the Hot-AXIOS-Stent® (Boston Scientific; n=1: 10x10mm, n=14: 15x10mm, n=18: 20x10mm). For this, the intestinal target loop was filled with fluids and subsequently directly punctured with the stent delivery system followed by stent release under endosonographic control.

Results: A total of 28 patients (50% men/50% women; mean age 66.5 years) underwent direct EUS-GE for gastroduodenal obstruction of malignant (n=24), benign (n=3) or unknown (n=1) etiology. The technical success rate of correctly placed LAMS was 96% (27/28). However, in 18 % of patients (5/28) the distal flange of the stent was unintendedly released in the peritoneal cavity due to loss of contact to the target loop while performing the first puncture but in 80% (4/5) of these cases correct stent placement succeeded in a second attempt. In one patient (1/5) no second EUS-GE-attempt was performed since prospects of success were limited due to ascites causing lacking target loop contact. Subsequently, surgical gastroenterostomy was performed in this case. After misplacement of the stent, the gastric perforation site was sufficiently closed by Over-The-Scope-Clipping (OTSC) in 2/5 cases or no further treatment was needed due to small defect size (3/5). 85% of the patients (24/28) benefited from the intervention by showing reduced nausea and vomiting and the ability of oral food intake. In one case placement of a second EUS-GE was necessary after technically successful first EUS-GE-intervention to achieve symptom relief and enable oral food intake. Another patient (1/28) developed a gastrojejunocolic fistula by accidental colon interposition during EUS-GE-intervention. This complication was managed by placing an esophageal stent reaching from the stomach through the colon into the jejunal target loop.

Conclusion: Direct EUS-GE with LAMS has a favorable risk-benefit-profile for patients with gastroduodenal obstruction showing high technical success rates, manageable complications and rapid symptom relief.

Disclosure: Nothing to disclose

P1345

MEDIUM-TERM FOLLOW-UP OF EUS GUIDED ANASTOMOSIS

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Introduction: EUS-guided anastomosis (EUS-A) with LAMS have emerged as a therapeutic option for patients with benign or malignant obstruction of the digestive tract.

Although the anastomotic site could theoretically be found in any part of the gastrointestinal tract, most of the reported cases involve the gastric wall and the small intestine, and experience in distal obstruction is limited to few case reports.

Also, the long-term permeability of these anastomoses after removing LAMS remains unknown.

Aims & Methods: Retrospective study between March 2018 to May 2020, describing the technical success according to the anastomotic site and long-term follow-up in those cases in which the stent was removed or migrated spontaneously.

Results: 37 cases were treated with LAMS. Mean age 67 years. Cause of obstruction: 34 maligns (91%) and 3 benign(9%). Thirty one LAMS had their proximal flange located in the gastric lumen, whereas in 6 (20%) the gastric wall was not involved. *Table 1.*

Technical success was achieved in 100% of transgastric procedures. Of 6 patients in whom a lower EUS-A was intended, 2 failures were recorded. In the other 4 patients (67%) we placed the LAMS successfully and without major complications. These cases include the following anastomosis:colo-rectal (1case), jejunojejunal (2 cases)and ileo- ileal (1 case). LAMS were removed in three patients (Figure 1). In one patient with entero-enteric and another with recto-colic anastomosis, stent removal after spontaneous displacement was followed by long term permeability of the EUS-guided anastomosis (240 and 510 days respectively). In a EUS-guided gastroenterostomy the stent was removed at 118 days, but closure of the fistula was confirmed 26 days later.

Characteristics of patients		GEA EUS-guided gastroenteroanastomosis n = 31	Percentage (%)	EEA EUS-guided anastomosis without involvement of the gastric wall n = 6	Percentage (%)
Obstruction side	Antral/Prepyloric	9	29%		
	2°-3° duodenal portion	22	70.96%		
	4° duodenal portion/jejunum			2	33.3%
	Ileum			3	50%
	Recto			1 (Colorectal disconnection)	16.6%
Type of obstruction	Malignant	29	93.5%	5	83.3%
Previous obstruction treatment	Yes (Duodenal prosthesis)	1	3.22%		
	Surgical GEA	3	9.67%		
	Abdominal surgery			5	83.3%

[Table 1]

Conclusion: Our experience suggests that LAMS placement between bowel loops is feasible in well-selected patients, although in our experience it requires more technical skill.

When LAMS are placed through the gastric wall, the removal of the stent seems to lead to the closure of the fistula.

When LAMS are placed between bowel loops, it might allow the creation of an anastomosis with long-term permeability.

In the future, well-designed RCTs and prospective studies are needed to further validate these findings.

Disclosure: Nothing to disclose

P1346

ARTIFICIAL INTELLIGENCE IN THE PREDICTION OF MALIGNANT POTENTIAL IN GASTROINTESTINAL STROMAL TUMORS OF STOMACH

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Introduction: Artificial intelligence (AI) is a novel approach in the diagnostic as well as therapeutic aspects of gastrointestinal diseases. We aimed to investigate whether AI via deep learning algorithm using endoscopic

ultrasonography (EUS) images could predict the malignant potential in gastric gastrointestinal stromal tumors (GISTs) according to the Armed Forces Institute of Pathology (AFIP) risk classification. We also evaluated several EUS features that might be correlated with malignancy.

Aims & Methods: A retrospective series of patients who underwent EUS followed by surgical resection for gastric GISTs between October 2010 and December 2019 at a tertiary referral center were included in this study. Fifty-five patients whose EUS images of GISTs were recorded in a digital format were analyzed. A total of 685 images were collected from 55 patients. Convolutional Neural Networks (CNNs) were constructed as a deep learning model. Synthetic Minority Oversampling Technique (SMOTE) was used to increase the number of the images to 1730. Seventy percent of the generated images was used for AI training and 30% was used to test AI diagnoses. For each tumor, the following EUS features were recorded: size, shape (non-distorted or distorted), presence of lobulation, regularity of extraluminal and intraluminal borders (regular or irregular), mucosal ulceration, echogenicity (iso/hypoechoic or hyperechoic), homogeneity (homogeneous or heterogeneous), anechoic spaces, hyperechoic foci, hypoechoic halo, and growth pattern (endoluminal or exophytic/mixed). The primary outcome was the prediction of malignant potential via AI using EUS images; secondary outcome was the association of EUS features with risk of malignancy.

Results: The mean age was 56.1 ± 12.3 years and 35 patients (63.6%) were female. Localization of GISTs were cardia 10, fundus 9, body 22, and antrum 14. While 52 originated from the fourth layer of the wall, remaining 3 from the second layer. The overall diagnostic sensitivity, specificity, and accuracy for predicting AFIP risk via AI were 83%, 94%, and 82% (Table 1). When patients divided, simply, into two risk groups, low-risk versus high-risk, sensitivity, specificity, and accuracy were 99%. In univariate analysis, none of conventional EUS features was a risk factor for predicting malignancy ($P > 0.05$). Fundus location was significant for predicting risk of malignancy ($P = 0.019$). Tumor size over 40 mm and fundus location were significant for predicting a high mitotic index ($P = 0.011$ and $P = 0.013$).

AFIP risk classification	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Very low-risk	56%	95%	81%	85%	
Low-risk	93%	95%	83%	83%	
Intermediate-risk	97%	94%	86%	99%	
High-risk	86%	92%	77%	95%	
Overall	83%	94%	82%	93%	82%
AFIP risk classification (very low-risk included in low-risk and intermediate-risk included in high-risk)					
Low-risk	99%	100%	100%	99%	
High-risk	100%	99%	99%	100%	
Overall	99%	99%	99%	99%	99%

[Diagnostic performance of AI for prediction of malignancy and mitotic index]

Conclusion: Our results showed that AI via deep learning algorithm using EUS images could predict the risk of malignancy in gastric GISTs with high accuracy.

Disclosure: Nothing to disclose

P1347 WITHDRAWN

P1348

INTEROBSERVER AGREEMENT OF ENDOSCOPIC ULTRASOUND ASSESSMENT AND MANAGEMENT OF PANCREATIC FLUID COLLECTIONS (PFCs) - AN INTERNATIONAL STUDY

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Introduction: Pancreatic and peripancreatic fluid collections (PFCs) are amongst the most ominous complications of severe acute pancreatitis (1) and in this field Endoscopic ultrasound (EUS) is as an accurate tool for diagnostic and therapeutic approach (2,3). However, a validate classification on EUS finding is lacking and controversies about EUS-guided treatment are still present.

Aims & Methods: Twelve experts in interventional EUS from 9 European and US tertiary endoscopy centers were invited to evaluate 50 EUS videos of pancreatic fluid collections and were asked to express their opinion on specific details of size, type, morphological signs and therapeutic decision. The primary endpoint was to assess the Interobserver agreement (IOA) among endosonographers for EUS diagnosis and classification of PFCs. The secondary endpoint was to evaluate their agreement about endoscopic and non-endoscopic drainage of fluid collections.

Results: A moderate agreement was found in terms of type of lesion ($k=0.49$) while a fair or poor agreement was stated for the presence of infection ($k=0.2079$), the evaluation of the wall of the PFC, the gut wall visibility, the distance from the PFC and the presence of interposed vessels ($k=0.1372$, $k=0.0375$ and $k=0.0557$, $k=0.2308$, respectively). Wirsung visibility and its communication showed poor agreement ($k=0.0579$ and $k=0.1271$, respectively). A fair agreement was also stated in terms of treatment ($k=0.3976$).

Conclusion: The diagnosis and management of pancreatic fluid collections by EUS-procedures are still based on single-center experience and there is no a good agreement between expert endosonographers. Further studies, guidelines and consensus are needed to establish a common evidence-based management in the Western endoscopic centers.

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Disclosure: Nothing to disclose

P1349

CUSUM ANALYSIS GUIDING MULTICENTER QUALITY IMPROVEMENT OF EUS-GUIDED TISSUE ACQUISITION OF SOLID LESIONS OF THE PANCREAS

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Introduction: With the development of neo-adjuvant therapy for pancreatic carcinoma, the role of endoscopic ultrasound (EUS)-guided tissue acquisition (TA) is becoming ever more important. The American Society for Gastrointestinal Endoscopy (ASGE) defined three quality indicators for EUS-guided TA: rate of adequate sample ((RAS), performance target 85%), diagnostic yield of malignancy ((DYM), performance target 70%) and sensitivity for malignancy ((SFM), performance target 85%). Cumulative sum (CUSUM) analysis is a statistical method that can be used to create learning curves of a (medical) process. Our research group QUEST (Quality in endosonography team) is a regional endosonography interest group that is working on improvement of the quality and yield of EUS-guided TA.

Aims & Methods: The aim of this study was to use CUSUM as a method to visualize changes in the quality and yield of EUS-guided TA in the contributing hospitals and overall in retrospect, and to evaluate whether ASGE performance targets are met.

Five community hospitals in the Rotterdam region, the Netherlands, participated in this study (in the table indicate with letters A to E). Each hospital retrospectively collected data of all consecutive EUS-guided TA of solid pancreatic lesions in 2013 and 2014. From January 2015 onwards, all five hospitals started a prospective registration of all consecutive EUS-guided TA procedures of solid pancreatic lesions. CUSUM curves were plotted for each individual hospital and for the complete cohort to detect changes in quality. We calculated the differences in RAS, DYM and SFM between before and after a possible change in quality and used the CUSUM curves to define that moment in time.

Results: In total we included 618 procedures of EUS-guided TA in five community hospitals. The value of RAS met the performance target of 85% for each hospital. DYM and SFM gradually improved in each hospital. Changes in CUSUM curves towards a horizontal or upslope curve were detected in all 5 hospitals. These changes occurred at different moments in time. Episodes before and after a positive change in CUSUM curves were compared regarding RAS, DYM and SFM overall and per hospital. Results are presented in table 1. Examples of specific interventions related to these changes were: introduction of ROSE in all cases, reduction in number of endosonographers/cytopathologists involved.

Hospital	Number of procedures	RAS	DYM	SFM
A before (May 2013 - June 2015)	45	38 (84%)	24 (53%)	55%
A after (June 2015 - June 2017)	45	39 (87%)	32 (71%)	78%
p-value of the difference		0.7	0.08	0.02
B before (Nov 2015 - Dec 2017)	36	30 (83%)	20 (56%)	65%
B after (Jan 2018 - Dec 2018)	36	34 (94%)	27 (75%)	87%
p-value of the difference		0.1	0.09	0.03
C before (July 2016 - Sept 2017)	26	26 (100%)	15 (58%)	71%
C after (Oct 2017 - Dec 2018)	26	25 (96%)	18 (69%)	82%
p-value of the difference		0.3	0.4	0.4
D before (Jan 2013 - Dec 2014)	40	30 (75%)	14 (35%)	40%
D after (Jan 2015 - Feb 2017)	40	40 (100%)	29 (73%)	85%
p-value of the difference		<0.01	<0.01	<0.01
E before (Jan 2013 - March 2016)	52	38 (73%)	17 (33%)	44%
E after (Apr 2016 - Dec 2018)	51	48 (94%)	39 (76%)	81%
p-value of the difference		<0.01	<0.01	<0.01
Total before (May 2013 - Feb 2018)	100	95 (95%)	64 (64%)	76%
Total after (March 2018 - Dec 2018)	100	94 (94%)	77 (77%)	86%
p-value of the difference		0.8	0.04	0.07

[Table 1. Values of RAS, DYM and SFM for each individual hospital and the complete cohort.]

Conclusion:

1. By providing visual feedback on performance, CUSUM analysis is a valuable tool guiding multicenter quality improvement and maintenance.
2. Although overall the ASGE performance measures are met, there is still room for further improvements in individual hospitals.

Disclosure: Nothing to disclose

P1350

ASA SCORE AND OBESITY, BUT NOT AGE, INCREASE COMPLICATIONS OF ENDOSCOPIST-BASED PROPOFOL SEDATION FOR EUS

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Introduction: Upper endoscopy interventional procedures make sedation a must. However, sedation for upper EUS can be challenging, because of the possibility of airway compromise, as well as the highly reflexogenic nature of the pharynx. This can be even worse in elderly, obese or in patients with comorbidities.

Aims & Methods: To study risks, safety and complications of endoscopist-guided propofol sedation for upper EUS in patients with comorbidities, obese or elderly.

Every patients referred for EUS to 'Virgen de las Nieves' University Hospital from January 2011 to May 2019 was included. Demographic data, baseline clinical data, indication, comorbidities, propofol dosage and complications were prospectively collected in a database. We compared complications between patients under 65 years old and older than 65, BMI < 35 and above 35, and patients classified as ASA 1 or 2, and the ones with ASA classification of 3 or 4. Baseline characteristics such as pulse, oxygen saturation

were compared. Main complications such as hypoxemia during or after the procedure, significant hypotension or clinically relevant cardiac rhythm abnormalities were compared between groups. Propofol dosage and times relevant to the procedure were also compared (induction of sedation, procedure time, and recovery time).

Results: 2975 patients underwent EUS between January 2011 and January 2019 (48,6% male). 1338 (45%) were older than 65 years, 743 (25%) were ASA III-IV and 27 (1%) were obese. Elder patients had a lower 46basal oxygen saturation (97%vs98,5%; $p < 0,0001$), so did ASA3-ASA4 patients (96,7%vs.98,1%; $p=0,005$). No differences were found in heart rate between those groups, nor in obese/lean patients. Propofol doses were significantly lower in old people ($p < 0,0001$), and ASA3-ASA4 ($p < 0,0001$). In obese patients, only the induction dose was different with respect to leaner patients, but not the reinjection doses ($p < 0,0001$). The bivariate analysis showed that older patients (3.6% vs. 2%; $p < 0.008$), ASA3-ASA4 patients (4.6%vs.2.19%; $p < 0.001$), and obese patients (26%vs.4.7%; $p < 0.01$) suffered desaturation more frequently. ASA3-ASA4 patients had also an increase rate of bradycardia (0.7% vs. 0.13%; $p=0.014$).

When considered all complications related with sedation (desaturation, bradycardia and hypotension) in a multivariate analysis, Obesity (OR: 8.57; CI95%: 3.62-20.28; $P < 0.0001$) and comorbidities (ASA3-ASA-4) (OR: 2.04; CI95%: 1.44-3.01) were independently related with them but not age, when corrected by the two other risk factors.

Conclusion: Comorbidities and obesity are risk factors for adverse events when sedating patients for EUS. Older patients need lower doses of sedatives, determining the other two factors but not age itself risk factors for complications.

Disclosure: This abstract was sent and accepted for the failed ESGE days 2020, Dublin

P1351

ENDOSCOPIC ULTRASOUND-GUIDED DRAINAGE OF PERIPANCREATIC FLUID COLLECTIONS - WHAT AFFECTS EFFICACY?

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Introduction: Peripancreatic fluid collections (PFC) are common complications of acute and chronic pancreatitis and should be drained in certain clinical situations. According to the Atlanta Classification of Acute Pancreatitis (revision 2012), PFC are divided into four distinct forms: acute peripancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection and walled-off necrosis.

Aims & Methods: The aim was to assess the efficacy and safety of endoscopic ultrasound (EUS)-guided endoscopic drainage of pancreatic pseudocysts and walled-off necrosis. This was a retrospective study of 64 patients with PFCs treated with EUS-guided drainage.

Results: Successful drainage (complete resolution of fluid collection) after a single procedure was achieved in 35 of 64 individuals (54.7%), and finally, in 55 of 64 patients after several procedures (85.9%). Drainage success after a single procedure was more likely in the case of PFCs present for > 3 months vs < 3 months (22/25 vs 12/20; OR = 4.89; 95% CI: 1.09 - 21.95; $p = 0.03$). In elderly patients or those with infection of the PFC or pancreatic fistula, a higher number of procedures had to be performed to achieve resolution (mean $\pm$ SD: 47 $\pm$ 15 y vs 55 $\pm$ 14 y; OR = 0.96; 95% CI: 0.92 - 1.00; $p = 0.02$; 4/33 vs 10/27; OR = 0.23; 95% CI: 0.06 - 0.86; $p = 0.02$ and 0/35 vs 6/27; OR = not applicable; $p = 0.005$; respectively). The total duration of PFC resolution was longer in patients with PFC localized to the head of the pancreas (135 $\pm$ 229 vs 59 $\pm$ 48 days; $p = 0.05$). The use of self-expandable

metallic stents compared with plastic stents was associated with a lower total number of stents used to treat a single patient (OR = 0.03; 95% CI: 0.01-0.29; $p = 0.0001$), but did not influence the total number of endoscopic procedures and the final success rate.

Complications were more frequent in patients with PFC <3 months vs >3 months from the acute episode (4/11 vs 1/34; OR = 18.86; 95% CI: 1.70 - 209.11; $p = 0.01$), in patients without underlying chronic pancreatitis (9/39 vs 1/25; OR = 7.20; 95% CI: 0.82 - 63.51; $p = 0.04$) and in case of large vs small PFCs - diameter >10 cm vs <10 cm - (8/28 vs 1/27; $p = 0.01$; OR = 10.4; 95% CI: 1.14 - 94.76).

Conclusion: EUS-guided drainage efficacy during a single procedure is related to the maturity of fluid collection, patient age, infection and pancreatic fistula formation. The duration and efficacy of endoscopic treatment are related to PFC localization in pancreas. The efficacy and safety of endoscopic EUS-guided drainage of PFC is associated with several factors, which should be considered in treatment planning.

Disclosure: Nothing to disclose

P1352

ENDOSCOPIC ULTRASOUND GUIDED THROMBIN INJECTION FOR BLEEDING PSEUDOANEURYSM : A NOVEL APPROACH

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Introduction: Pseudoaneurysm usually occurs after vascular injuries or erosions after in trauma or inflammation like pancreatitis and associated with high morbidity and mortality. Digital subtraction angiography with coil embolization is established treatment for aneurysm. There is paucity of data in literature on endoscopic ultrasound (EUS) guided thrombin injection for pseudoaneurysm. Probably this is the largest prospective study of use of thrombin in bleeding pseudoaneurysm.

Aims & Methods: Aim of study is to assess efficacy and safety of EUS guided thrombin injection in bleeding pseudoaneurysm.

Prospective data collection was done at SMS Hospital, Jaipur from January 2015 to December 2019. All patients with pseudoaneurysm with history of upper gastrointestinal bleed were consecutively enrolled. Data relating to demography, laboratory parameters, radiological imaging, and endotherapy were analyzed.

Results: Eighteen patients (M:F-17:1) with median age 39.5(22-58) years, were studied. Underlying etiology of pseudoaneurysm was chronic pancreatitis in 14 (77.7%) patients, blunt trauma abdomen in 3 (16.6%) patients, acute pancreatitis in 1 (5.5%) patient.

At the time of admission median hemoglobin was 6.4 gm/dl (4.2-9.3), with median blood transfusion requirement was 2 unit (1-4). Median dose of human thrombin required for complete obliteration of pseudoaneurysm was 500 IU(300-800). Computed tomography (CT) and EUS after 4 weeks and 3 months showed obliterated pseudoaneurysms in 17 (94.44%) patients, while recurrence was seen in 1 (5.55%) patient at 6 weeks of thrombin injection, one patient developed splenic abscess post thrombin injection requiring splenectomy.

Conclusion: EUS-guided thrombin injection provides a new option for management of bleeding pseudoaneurysm.

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Disclosure: Nothing to disclose

P1353

EUS-GUIDED CYANOACRYLATE INJECTION VERSUS STANDARD ENDOSCOPIC TECHNIQUE IN THE TREATMENT OF HIGH RISK GASTRIC VARICES

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Introduction: Endoscopic variceal obliteration (EVO) by direct endoscopic injection (DEI) using tissue adhesives like cyano-acrylate (CYA) has been advocated as first-line method in managing gastric varices (GVs). Nevertheless, CYA is known to be associated with significant adverse events like post injection ulcer, needle sticking in the varix, adherence of the glue to the endoscope, and embolization into pulmonary or systemic vessels. Targeting the perforating feeding vessel by EUS rather than the varix lumen itself may theoretically minimize the amount of CYA needed to achieve obliteration of GV and thereby reduce complications.

Aims & Methods: The aim of the study is to compare the efficacy & safety of EUS-guided CYA injection into the perforating vein versus DEI of CYA in treatment of high risk gastric varices. This is a single center pilot study that included 42 patients with high risk GV larger than 10 mm. Eligible patients were randomized in 2 groups (21 patients in each group) using computer-generated random number sequences in concealed envelopes.

Group I underwent EUS-guided injection of 1ml CYA into the perforator vein and Group II underwent DEI of 1 ml CYA into the varix. Obliteration of GV by Doppler EUS was considered by visualization of clot and absence of Doppler flow within the varix. Repeat injection was performed in the absence of obliteration. Direct endoscopic and Doppler EUS examinations were repeated again at 3, and 6 months after each injection.

Results: From February 2019 to February 2020, 21 out of 42 patients with GV were treated. For Group I; 13 patients were treated, from which 2 patients dropped out on follow up. There was 7 females and 4 males. Their median age was 56 years (34-69). At index endoscopy, the mean size of GV was 41 mm (27-61) which decreased to 19 mm (11-32) at 3 months of follow up with obliteration of GV in 9 out of 11 patients. 2 patients were re-injected with obliteration at further 3 months of follow up. For Group II, 8 patients were treated, from which 1 patient dropped out on follow up.

There was 1 female and 6 males. Their median age was 53 years (46-60). At index endoscopy, the mean size of GV was 30 mm (21-47) which decreased to 20 mm (10-36) at 3 months of follow up with obliteration of GV in 3 out of 7 patients. 4 patients were re-injected with obliteration in 1 patient at further 3 months and 3 patients still waiting follow up.

No complications were reported in Group I compared to self-limited bleeding in 3 patients, post injection ulcer in 2 patients and needle sticking in 1 patient in Group II.

Conclusion: EUS-guided CYA injection into the perforating vein is effective method for obliteration of high risk GV requiring less number of sessions with less complications compared to conventional DEI.

Disclosure: Nothing to disclose

P1354

FEASIBILITY AND SAFETY OF EUS-GUIDED PLACEMENT OF FIDUCIAL MARKERS FOR STEREOTACTIC BODY RADIATION THERAPY IN PANCREATIC CANCER: A PROSPECTIVE AND QUALITATIVE EVALUATION

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Introduction: In patients with borderline resectable or locally advanced pancreatic ductal adenocarcinoma (PDAC), stereotactic body radiation therapy (SBRT) is a new neoadjuvant treatment option, allowing the delivery of higher equivalent biological dose directly to the tumor/vessels interface, while reducing damage to the adjacent organs.

The insertion of radiopaque markers in or close to the tumor is a prerequisite for this technique in order to precisely localise the target and track the tumor motion. Endoscopic ultrasound (EUS) placement of fiducial markers in PDAC is currently the preferred route of insertion.

Aims & Methods: We aimed to assess the feasibility and safety of EUS-guided fiducial placement in our two academic centres, as well as to evaluate both the technical and quality success of this technique, from both the endoscopist's and radiotherapist's points of view. We prospectively collected clinical and technical data concerning all the PDAC patients submitted to EUS-guided placement of fiducial markers and treated with SBRT.

"Technical success" was defined as at least one marker presumed to be inside the tumour at the end of the EUS procedure.

"Quality success" was measured using a newly score created in collaboration with the radiotherapist, which included the following criteria: number of markers inside or <1 cm from the tumour, number of markers located in the extremity of the tumour, their location in different planes, their distance from the biliary stent (if present) and the distance between the fiducials (if more than one visible marker)).

"High quality success" was defined as a score equal or higher than 6/12 points.

Results: From February 2018 to November 2019, a total of 37 patients were enrolled. The majority were male patients (54.1%), with a median age of 60 year old (IQR 18). The mean tumor size was 25.9 mm (SD 7.7) and lesions were mostly located at the pancreatic head (70%). The vast majority of the lesions were considered borderline resectable or locally advanced, with only one showing no vascular involvement (60% and 35% had venous and arterial vessels involvement, respectively). A total of 97 fiducials were implanted, with a median number of 3 fiducials placed per patient (range 0-4). The technical success rate was 92%, with failure of fiducials placement in 3 patients, mostly due to interposing vessels or difficulty to define the tumor limits (altered by the induction chemotherapy).

Adverse events were observed in three patients (8%), with 1 case of post-procedural fever, 1 case of mild acute pancreatitis and 1 case of biliary stent migration. All the patients that had fiducial markers placed could receive SBRT treatment, even though markers migrated in 2 patients.

From the other 32 patients, 76 % had at least 2 markers inside or less than 1 cm from the tumor and in 75% there was at least one marker located in the extremity of the tumor. Nevertheless, markers placement in different spacial planes was achieved in only 56% of the cases and there were 72% were at least 2 markers were positioned to close from each other. The high quality success rate was 62.5%.

Conclusion: Our results confirm the feasibility and security of EUS-guided fiducial markers placement for SBRT treatment in PDAC, with encouraging results regarding technical success and the rate of adverse events. The newly proposed quality score will hopefully lead the way for improvement in fiducials positioning, potentially contributing for a better SBRT treatment delivery with better final results.

Disclosure: Nothing to disclose

P1355

SINGLE-SESSION ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PLUS ENDOSCOPIC ULTRASOUND-GUIDED GALLBLADDER DRAINAGE THROUGH LUMEN APPOSING METAL STENT, FOR CHOLECYSTOLITHIASIS WITH ACUTE CHOLECYSTITIS AND CONCOMITANT CHOLEDOCHOLITHIASIS IN PATIENTS UNFIT FOR SURGERY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP), followed by laparoscopic cholecystectomy, remains the gold standard for the management of cholecysto-choledocholithiasis. Laparo-endoscopic rendezvous, which combines laparoscopic cholecystectomy and ERCP at the same time, is a valid alternative.

However, due to advanced age and multiple comorbidities, many patients are often unfit for surgery. Recently, endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) using lumen apposing metal stents (LAMS) has been increasingly used.

Furthermore, a novel dedicated fully-covered and electrocautery-enhanced LAMS (Hot Axios™, Boston Scientific, Marlborough, United States) has been developed.

Aims & Methods: This prospective study aims to evaluate the effectiveness and safety of an ERCP plus EUS-GBD through LAMS, in a single-session, for cholecystolithiasis with acute cholecystitis and concomitant choledocholithiasis in patients unfit for surgery for advanced age and comorbidities. Eighteen patients (7 women, 11 men) unfit for surgery, with a median age of 86 years (range 76-90), who presenting cholecystolithiasis with acute cholecystitis and concomitant choledocholithiasis, were consecutively enrolled.

All patients underwent ERCP plus EUS-GBD through LAMS in a single-session, over a one-year period (January 2019 - January 2020). First, an ERCP was performed for common bile duct stones' removal. Immediately after, an EUS-guided gallbladder drainage, creating a cholecystogastrostomy or a cholecystoduodenostomy, was performed using the Hot Axios™ system. Primary outcomes were technical and clinical success. We also recorded the adverse events rate and stent patency.

Results: The median procedure time was 40 minutes (range 28-52). Either for ERCP and for EUS-GBD, the technical and the clinical success was obtained in all patients (18/18, 100%), without peri-procedural complications, and stent patency was good in all of them (using 10x10 mm or 15x10 mm LAMS). LAMS was removed four weeks after placement, in patients with good life expectancy, otherwise it was left indefinitely.

Starting from LAMS' placement, median follow-up time was 67 days (range 28-365), assessed by abdomen computer tomography (CT-scan), without complications during follow-up. No complications as "buried stent" were observed at the moment of LAMS' removal. None of the patients needed reintervention, due to the absence of disease recurrence in all of them.

Conclusion: Despite the small number of patients in our study, the endoscopic alone management of cholecystolithiasis with acute cholecystitis and concomitant choledocholithiasis, performed in a single-session with ERCP plus EUS-GBD through LAMS, has high technical and clinical success rates and shows very low complications and reintervention rates in patients unfit for surgery, that are the best candidates. Further prospective and larger studies are needed.

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Disclosure: Nothing to disclose

P1356

INTERMITTENT VERSUS CONTINUOUS SUCTION TECHNIQUE FOR THE DIAGNOSIS OF PANCREATIC SOLID LESIONS. A PILOT STUDY

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Introduction: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is the method of choice for sampling pancreatic solid lesions. However, there is a significant heterogeneity in terms of the used technique. Intermittent suction has not been evaluated on prospective studies and might improve diagnostic yield of EUS-FNA in pancreatic solid lesions.

Aims & Methods: A pilot single-blinded non-inferiority trial was performed. Consecutive patients with pancreatic solid lesions and indication of EUS-FNA were prospectively included.

Patients were randomized to intermittent (IS) and continuous (CS) suction. EUS-FNA were performed with a 25-gauge needle and 10 ml suction syringe, with four passes, without on-site pathologist. Specimens were pushed out using a stylet and sent to the pathologist on slides (passes 1-4), and a 5 ml syringe with Thinprep liquid medium was used to push remnant material to assess the presence of cell-block.

Diagnostic yield, cellularity (Grade 0: scant, Grade 1: adequate, Grade 2: excellent), blood contamination (Grade 0: low, Grade 1: moderate; Grade 2: significant) and number of passes needed to reach final diagnosis were evaluated.

Results: 33 pancreatic lesions were randomized to EUS-FNA and continuous (16 lesions) or intermittent (17 lesions) suction. Diagnostic yield was 87,5% in the CS and 94,1% in the IS, but there were no significant differences between both techniques (OR 2,29, IC95% 0,19-27,99, p = 0,51). In the IS group, samples had higher cellularity (OR 1,83, IC95% 0,48-6,91) and less blood contamination (OR 0,38, IC95% 0,09-1,54), but neither reached statistical significance (p = 0,37 and p = 0,18 respectively).

The number of passes needed to reach diagnosis were 2,12 with CS and 1,94 with IS (p = 0,64). Cell-block was obtained in 61,5% of CS and 73,3% of IS, but differences were not significant (OR 1,72, IC95% 0,35-8,50).

Lesions (N = 33)	Continuous suction (N = 16)	Intermittent suction (N = 17)	P-value
Diagnostic yield, n. (%)	14 (87,5)	16 (94,1)	0,601
Cellularity, n. (%)			0,154
- Scant	5 (31,2)	1 (5,9)	
- Adequate	6 (37,5)	11 (64,7)	
- Excellent	5 (31,2)	5 (29,4)	
Blood contamination, n. (%)			0,439
- Low	4 (25)	8 (47,1)	
- Moderate	10 (62,5)	8 (47,1)	
- Significant	2 (12,5)	1 (5,9)	
Mean of passes to reach diagnosis, n ± SD	2,1 ± 1,3	1,9 ± 0,9	0,640
Cell-block (Thinprep)	8 (61,5)	11 (73,3)	0,689

[Final results comparing continuous suction and intermittent suction technique]

Conclusion: The intermittent suction technique was not-inferior in terms of diagnostic accuracy and provides EUS-FNA samples with a tendency to obtain higher cellularity, slight blood contamination and frequent presence of cell-block in the evaluation of solid pancreatic lesions compared to continuous suction. Further studies are needed to confirm our results.

Disclosure: Raquel Herranz Pérez has received research funding from Boston Scientific.

P1357

ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY OR HEPATICOASTOMY FOR AFFERENT LOOP SYNDROME: A RETROSPECTIVE COMPARISON WITH PERCUTANEOUS DRAINAGE

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Introduction: Afferent loop syndrome may complicate Billroth II or Roux-en-Y reconstructions over time and in general implies oncological disease recurrence. Where palliative surgery or percutaneous drainage (PTD) used to be the only option, endoscopic ultrasound (EUS)-guided drainage by gastroenterostomy (EUS-GE) has been gaining ground. Moreover, EUS can also provide biliary drainage by creation of a hepaticogastrostomy (EUS-HG), although data on this approach are even more scarce in this specific context.

Aims & Methods: Our aim was to revise our experience in using EUS or PTD for the management of patients with afferent loop syndrome and provide comparative data on the different approaches. The institutional database was queried for all consecutive minimally invasive procedures for afferent loop syndrome. EUS-HG, EUS-GE and PTD were separately analyzed. Efficacy, safety, hospital stay, effect on oncological therapy and overall survival were compared.

Results: In total, 13 patients were included (median age 60 years (IQR 50-64), 30.8% female), of which 5 patients (38.5%) were treated with PTD and 8 patients (71.5%) by EUS. In the EUS group, 4 patients underwent EUS-GE, using a transgastric electrocautery-enhanced lumen-apposing metal stent, and in 4 patients EUS-HG was performed. Baseline characteristics, such as age, sex, underlying disease, disease stage and mean follow-up

duration did not differ at baseline. Technical success was achieved in all patients. Using the ASGE lexicon, mild, moderate, severe and fatal adverse events did not occur in the EUS group, compared to 40%, 20%, 0% and 0% respectively in the PTD group ($p=0.035$). Clinical success, i.e. reduction of cholestasis or resolution of infection, was achieved in all patients undergoing the EUS guided approaches versus 80% in the PTD group ($p=0.385$).

Furthermore, higher rates of bilirubin decrease were seen amongst the EUS treated patients: >30% bilirubin decrease in 7 vs. 1 patient(s) in the PTD group ($p=0.032$), with >60% and >90% decrease identified only amongst EUS treated patients. Evaluation of procedure time, mean hospital stay, re-intervention rate, chemotherapy (re-)initiation rate, one-year survival and dysfunction rate did not reveal significant differences.

Considering the two different EUS approaches, EUS-HG and EUS-GE both showed perfect technical and clinical success rates, as well as almost identical safety profile and long term outcomes. And last, time to dysfunction analysis revealed similar results amongst the EUS-HG, EUS-GE and PTD treated patients (424 vs. 148 vs. 111 days, $p=0.121$).

Conclusion: In the management of afferent loop syndrome, EUS and PTD provided similar technical and clinical efficacy. Besides the obvious disadvantages of percutaneous drainage (eg. presence of an external drain), EUS led to significantly more bilirubin decrease and less adverse events compared to PTD. We furthermore showed that EUS-guided hepaticogastrostomy and gastroenterostomy provided similar outcomes, and may therefore be used interchangeably in this specific context.

Disclosure: Schalk van der Merwe holds the Cook chair in Interventional endoscopy and holds consultancy agreements with Cook, Pentax and Olympus. Wim Laleman co-chairs the Boston-Scientific Chair in Therapeutic Biliopancreatic Endoscopy with Schalk Van der Merwe and has consultancy agreements with Boston Scientific and Cook. Hannah van Malenstein holds a consultancy agreement with Boston-Scientific

P1358

TRANSESOPHAGEAL EUS-GUIDED CORE BIOPSY OF LUNG MASSES USING 22G FRANSEEN-TIP NEEDLE- INITIAL EXPERIENCE

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Introduction: EUS is well established modality for evaluation and sampling of solid and cystic lesions in the abdominal cavity and for screening patients with lung cancer for mediastinal lymph node metastasis. The utility of EUS- guided transesophageal core biopsy of lung tumors has been rarely investigated. Most prior reported cases were performed with fine-needle aspiration or with smaller caliber FNB- needles.

Aims & Methods: Objectives: To evaluate the diagnostic utility and safety of transesophageal EUS-guided core biopsy of pulmonary tumors using 22G Franseen-tip needle.

Methods: Data was collected retrospectively from January 2019 to October 2019. All the patients had pulmonary masses close to or abutting the esophagus, detected on CT-scan. They were referred for EUS- guided biopsy after failure of bronchoscopy to establish tissue diagnosis or judged as unsuitable for bronchoscopy due to the location. Patients underwent endoscopic ultrasound with a linear scope (Fujifilm EG-580UT) and fine needle biopsy using 22G Acquire needle (Boston Scientific Corp.). The obtained material was assessed visually by the endoscopist without onsite cytologist.

Results: Eleven patients (7 men, 4 women) underwent EUS-guided transesophageal core biopsy of lung masses during the study period. The pro-

cedure yielded tissue for histologic diagnosis in 100% of patients. Immunohistochemical analysis was possible in all cases. Non-small-cell lung cancer was proven in seven patients, small-cell lung cancer in two, metastatic lung disease in one and mesothelioma in one. No complication was encountered during the first 48 hours and after 30 days follow-up.

Conclusion: EUS- guided core biopsy of lung masses using 22G Franseen-tip needle is safe and established histologic diagnosis in all patients in this study. In cases of accessible lesions this procedure could be discussed as first-line diagnostic tool.

Disclosure: Nothing to disclose

P1359 WITHDRAWN

P1360

ENDOSCOPIC ULTRASOUND (EUS) IN OBSTRUCTIVE JAUNDICE PROVIDE ACCURATE LOCALIZATION AND TISSUE SAMPLING OVER CT, MAGNETIC RESONANCE IMAGING. AND ERCP: A COMPARATIVE STUDY

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Introduction: The causes of obstructive jaundice are varied, but it is most commonly due to choledocholithiasis, benign strictures of the biliary tract, pancreaticobiliary malignancies and metastatic diseases. Endoscopic Retrograde Cholangiopancreatography (ERCP) and Magnetic resonance cholangiopancreatography (MRCP) is widely used in the diagnosis and treatment of biliary and pancreatic disorders with several limitations and contraindications Endosonography (EUS) is a less-invasive modality, safe and can determine exactly the nature, location and site of the biliary obstruction in relation to the ampulla of Vater.

Furthermore histological nature in suspected malignant obstruction can be obtained by EUS fine needle aspiration (FNA) technique.

Aims & Methods: The aim of the study is to compare diagnostic performance between EUS, MRCP, ERCP and computed tomography (CT) in benign and malignant obstructive jaundice. This study was carried on 84 patients with obstructive jaundice and were classified into : Group (1): composed of 52 patients with suspected benign obstructive jaundice Group (2)composed of 32 patients with suspected malignant obstructive jaundice. CT, MRCP, ERCP, and EUS were done for all patients.

Results: Outcome of our results showed two groups of patients :(group 1) Choledocholithiasis 29 patients (34.5%) and (group2) biliary strictures 55 patients (65.5%), the latter divided into CBD stricture21(25%) , pancreatic head cyst 12(14.2%), pancreatic head mass 19(22.6%) and ampullary tumor 3(3.5%).

In Choledocholithiasis the sensitivity (S), specificity(Sp),positive predictive value (PPV), negative predictive value (NPV) and accuracy of EUS were (100%, 98.1%, 96.6%, 100%, and 98.8%) respectively, while for CT were(75.8%, 100%, 100%, 88.7%, and 91.6%) respectively but for MRCP were(93.1%, 98.1%, 96.4%, 96.4%, and 96.4%) respectively considering ERCP as gold standard.

In Common bile duct Stricture ERCP was the gold standard . The S, Sp, PPV, NPV and accuracy of MRCP was (90.5%, 100%, 100%, 96.9%, and 97.6%) respectively, while for EUS was (81%, 100%, 100%, 94%, and 95.2%) respectively. EUS FNA showed 14 cases benign stricture, 5 cases of cholangiocarcinoma and 2 cases of Non Hodgkin lymphoma.

In pancreatic head cyst group both MRCP and MRI were the gold standard. The S, Sp, PPV, NPV and accuracy of EUS were (100%, 100%, 100%, 100%, and 100%) respectively while for CT were (75%, 100%, 100%, 96%, and 96.4%) respectively. EUS FNA revealed 5 cases pancreatic pseudocyst, one case of tuberculous pancreatic cyst, one case of pancreatic serous cystadenoma, one case of pancreatic serous cystadenocarcinoma two cases of pancreatic mucinous cystadenocarcinoma and two cases of Intraductal papillary mucinous neoplasm.

In pancreatic head mass group both MRCP and MRI were the gold standard. The S, Sp, PPV, NPV and accuracy of EUS were (100%, 100%, 100%, 100%, and 100%) respectively while for CT were (63%, 100%, 100%, 91.5%, and 91.6%) respectively. All cases were pancreatic adenocarcinoma by EUS FNA.

In ampullary tumors group both MRCP and MRI were the gold standard. The S, Sp, PPV, NPV and accuracy of EUS were (100%, 100%, 100%, 100%, and 100%) respectively while for CT were (33.3%, 100%, 100%, 97.5%, and 97.6%) respectively. EUS FNA revealed one case of papillary adenoma and two cases of papillary carcinoma.

Conclusion: Endoscopic Ultrasound has high diagnostic performance with accurate localization of the site of biliary obstruction, minimal procedure complications and tissue sampling acquisition which helps effectively to differentiate between benign and malignant obstructive jaundice.

Disclosure: Nothing to disclose

P1361

IS ENDOSCOPIC ULTRASONOGRAPHY EXAMINATION NECESSARY IN PATIENTS OF EARLY ESOPHAGEAL SQUAMOUS CELL CARCINOMA BEFORE ENDOSCOPIC SUBMUCOSAL DISSECTION?

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Introduction: Esophageal squamous cell carcinoma (ESCC) ranked the seventh most frequent cancers, and is the fifth leading cause of cancer death in Taiwan. The overall 5-year survival rate of ESCC is 12-15%. It is important to diagnose ESCC in early stage and receive curative treatment. Endoscopic submucosal dissection (ESD) is a well-developed skill to complete resect gastrointestinal (GI) tract early cancer. The absolute indication of ESD for ESCC is cancer limited to mucosal layer, because of increasing the risk of lymph node metastasis (10-45 %) of ESCC when cancer invasion into submucosal layer.

Endoscopic ultrasonography (EUS) is an examination for detecting the invasion depth (T stage) of GI tract cancer, the reported accuracy of T1 stage is around 85% of ESCC, however, the result of detail discrimination of EUS among each subdivision of mucosa (T1a) or submucosa (T1b) is unsatisfied.

Aims & Methods: The aim of this study is to evaluate the accuracy of T1 stage subdivision of ESCC by higher frequency EUS probe prior to ESD treatment.

Results: Total 123 patients enrolled in this study and there were 106 patients with T1a and 17 were T1b stage of ESCC by EUS. After ESD treatment, all specimens were confirmed as T1 on pathology, EUS stage of T1a in 106 patients and 84 (79%) were confirmed as T1a, twenty two (21%) were T1b on pathology; of 17 T1b (patients refuse surgery) on EUS, 6 (35%) were confirmed as T1a and 11 (65%) were T1b on pathology, further subdivision of pathological T1a: 90 (m1: 40, m2: 22, m3: 28), and T1b: 33 (>m2: 23). The sensitivity, specificity, positive predictive value and negative value

of EUS T1a is 93%, 33%, 79% and 63%, respectively. All the patients with pathological T1b stage received further esophagectomy or concurrent chemoradiotherapy if surgery unfit.

Conclusion: EUS demonstrates excellent accuracy for T1a diagnosis, but low accuracy of distinguishing between stages T1a and T1b of ESCC. Even with high frequency miniprobe (20 MHz), the main cause of understage of T1b is difficult to detect the cancer micro-infiltration into submucosal layers, and peritumoral inflammation or submucosal fibrosis causes some difficulties in differentiating mucosal from submucosal lesions is the reason of overstage of T1a. To improve the diagnostic accuracy, developing advanced EUS device and more experience endoscopist are needed. Comparing with other locoregional staging method, EUS remains a valuable tool of detecting ESCC T1a stage when ESD treatment is considered.

Disclosure: Nothing to disclose

P1362

COMPARISON OF HISTOLOGICAL QUALITY BETWEEN 22-GAUGE FINE NEEDLE ASPIRATION AND FINE NEEDLE BIOPSY OF SOLID PANCREATIC LESIONS

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Introduction: Regarding pancreatic lesions, most studies comparing EUS-FNA (endoscopic ultrasound guided fine needle aspiration) and EUS-FNB (endoscopic ultrasound guided fine needle biopsy) have shown no difference in term of diagnostic accuracy. Few studies have assessed the quality of histological sample obtained with each needles. Yet, the amount of histological sample is crucial to the diagnosis of some pancreatic lesions. Besides, a large amount will be necessary in the future for personalized medicine.

Aims & Methods: The aim of the present study was to compare the histological quality of samples obtained with EUS-FNA and EUS-FNB for pancreatic solid lesion accessible with endoscopic ultrasound (EUS).

We performed a retrospective study in a single tertiary center. Using a hospital database, we included all consecutive patients who underwent EUS-guided sampling procedure of a pancreatic lesion from January 2017 to October 2018, with either a 22G FNA needle or a 22G FNB needle. For each sample obtained, cellularity was automatically determined, and all core tissues were manually delineated for area measurement using an image processing program. Diagnostic accuracy for malignancy of each needle was also determined, and adverse events were recorded.

Results: Eighty-eight patients met the inclusion criteria. Among them 40 (45.5%) underwent EUS-FNA and 48 (54.5%) underwent EUS-FNB. A core tissue was obtained in 15/40 (37.5%) of the cases in the EUS-FNA group versus 42/48 (87.5%) in the EUS-FNB group ($p < 0.005$). When we only compared patients for those a core tissue was obtained, the mean area of the total core tissue obtained was $0.4 \pm 0.7 \text{ mm}^2$ the EUS-FNA group and $2.8 \pm 3.3 \text{ mm}^2$ in the EUS-FNB group ($p=0.005$). EUS-FNA samples had a mean cellularity of $40740.4 \text{ cells} \pm 73243.0$ versus 25987.8 ± 45861.7 for EUS-FNB samples without statistical significance ($p=0.3$). In the EUS-FNA group, sensitivity and specificity for malignancy were 85.3% and 100% respectively and were not statistically different in the EUS-FNB group (92.5% and 100% respectively). Positive predictive value and negative predictive value in the EUS-FNA group were 100%, and 28.6% respectively versus 100%, and 57.1% in the EUS-FNB group. In the EUS-FNA group, 4 (10.0%) cases of immediate minor hemorrhages were observed. No adverse event

was observed within 30 days after the endoscopic procedure. In the EUS FNB group, no adverse event was observed either during the procedure or within 30 days after the endoscopic procedure.

Conclusion: In our study, FNB allowed to obtain a core tissue in near 90% of the cases which is twice more often than with FNA. The mean area of the core tissue obtained with FNB was 7-fold bigger than those obtained with FNA. In the future, more tissue would be necessary to perform molecular analysis allowing personalized medicine, FNB should be the needle of choice to obtain a large amount of pancreatic tissue.

Disclosure: Julien Branche received lecture fees from Cook, Boston, Life Europe. The other authors have no conflict of interest.

P1363

COMPARISON OF ENDOSCOPIC ULTRASOUND-GUIDED THROUGH-THE-NEEDLE BIOPSY AND NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY IN PATIENTS WITH PANCREATIC CYSTIC LESIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Pancreatic cystic lesions (PCLs) are frequent incidental findings on cross-sectional imaging and the risk of malignancy in different types of PCLs is dissimilar. Current preoperative stratification is only moderately accurate, resulting in a substantial number of low-risk lesions undergoing surgery [1]. Two novel diagnostic tools used in conjunction with endoscopic ultrasound and 19G needles have been recently introduced: through-the-needle biopsy (TTNB) and needle-based confocal laser endomicroscopy (nCLE) [2,3]. Both methods were shown to outperform aspiration cytology and carcinoembryonic antigen levels in cyst fluid. However, data comparing the two methods are currently lacking.

Aims & Methods: The aim of this meta-analysis was to compare TTNB with nCLE in patients with PCLs. Medline, Embase, Web of Science and Cochrane Library databases were searched in accordance with PRISMA statement and studies with five or more patients undergoing either EUS-TTNB or EUS-nCLE were included. Reviews, case reports, editorials, conference abstracts, and studies on exclusively solid pancreatic lesions were excluded. Literature search, assessment of study inclusion, data extraction, and quality assessment was performed independently by two authors. Outcomes of interest were diagnostic yield (defined as a proportion of cases where a diagnosis was established), sensitivity and specificity for distinguishing between mucinous and non-mucinous lesions, as well as concordance rates with definitive surgical diagnosis, safety, and technical success. Adverse events (AEs) were defined according to ASGE's Lexicon [4].

Results: Twenty studies with 1023 patients were included in the meta-analysis. The majority of the studies were single-center (n=12, 60%) and retrospective by design (n=11, 55%). Pooled diagnostic yield of EUS-nCLE was significantly higher compared to EUS-TTNB (85% vs. 74%, $p < 0.0001$), while diagnostic performance was high and comparable for both methods (sensitivity: 92% vs. 90% and specificity: 100% vs 96% for TTNB and nCLE respectively, $p > 0.05$). Concordance with the final diagnosis in the surgical subgroup (104 patients) was 82% (95%CI: 72-91%) and 65% (95%CI: 36-91%) for the TTNB and nCLE groups, respectively.

However, the difference was statistically insignificant due to a small sample size ($p=0.21$). Overall AE rate was 5% in TTNB-group and 3% in nCLE-group, $p=0.302$. Adverse events were mainly mild; but moderate (nCLE: 1.5%, TTNB: 1.3%) and even severe AEs (nCLE: 0.0%, TTNB: 0.7%) occurred. Most common AE was pancreatitis (nCLE: 2.1%, TTNB: 3.9%), followed by intracystic hemorrhage (nCLE: 0.4%, TTNB: 2.4%) and infection (nCLE: 0.4%, TTNB: 0.4%).

Meta-regression did not show any association between study design and quality, patient age or lesion size, and AE rate. Technical success rates were high and comparable (94% and 99% for EUS-TTNB and EUS-nCLE, respectively; $p=0.07$).

Conclusion: The two techniques are comparable in terms of technical success, sensitivity, specificity, while EUS-nCLE demonstrated a higher diagnostic yield. EUS-TTNB and EUS-nCLE had similar safety profile with slightly higher AE rate compared to EUS-FNA. Limits of this meta-analysis are the relatively small proportion of patients who underwent surgery and had a confirmatory diagnosis and the retrospective design of most of the included studies.

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P1364

LESSONS LEARNED FROM CUSUM ANALYSIS OF EUS-GUIDED TISSUE ACQUISITION OF SUSPECTED PANCREATIC CANCER

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Introduction: Endoscopic ultrasound (EUS)-guided tissue acquisition (TA) is the method of choice to establish a pathological diagnosis of solid pancreatic lesions. EUS-guided TA is a complex multistep procedure involving efforts of both endosonographers and cytopathologists. Practice variation regarding quality and yield of these procedures amongst community hospitals is an unwanted but existing phenomenon as we previously showed in our regional endosonography interest group QUEST (quality in endosonography team) (1).

In order to reduce this practice variation and improve our quality, we organize three annual meetings during which we discuss our performances, overall and per hospital, and determine best practices. Diagnostic Yield of Malignancy (DYM) is one of the ASGE defined quality indicators for these procedures with its minimum target value set at 70% (2).

Cumulative sum (CUSUM) analysis is an established tool to evaluate endoscopy trainees by graphically plotting their performance development over time (3). Similarly, CUSUM can be used to visualize DYM over time as a tool to provide feedback per hospital and continuously measure quality.

Aims & Methods: Aim of this study was to compare the CUSUM curves of the hospitals in QUEST and to find an explanation for possible changes in the curve. We prospectively collected data of EUS-guided TA procedures from 5 regional community hospitals from 2015-2019. A total of 463 consecutive EUS-guided TA procedures were included. CUSUM curves of DYM, using 70% as a minimum target value, were created in retrospect for all hospitals combined and per hospital.

Results: The overall CUSUM curve of DYM shows a gradual improvement over the years after the formation of QUEST indicating its positive effect on quality improvement. However, the CUSUM curve of one of the participating hospitals revealed a temporal but remarkable negative change in the quality of DYM during an episode of 4 months in 2017. Analysis of potential explanations for this change revealed a sudden increase in the number of diagnoses of atypia related to a temporal absence of one of the more experienced cytopathologists.

Conclusion: CUSUM analysis is an easy-to-use tool to continuously monitor quality and guide quality-improvement of EUS-guided TA of solid pancreatic lesions. Variations in the curve, in particular when a negative trend develops, should trigger further analyses to identify the culprit and to instigate corrective actions.

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P1365

DO ENDOSONOGRAPHERS AGREE ON THE PRESENCE AND SUBSEQUENT NEED FOR TREATMENT OF BILE DUCT SLUDGE?

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Introduction: Endoscopic ultrasonography (EUS) is an excellent tool to prevent unnecessary therapeutic Endoscopic Retrograde Cholangiography (ERC) and its complications in patients with suspected common bile duct (CBD) lithiasis(1). In these patients EUS detects sludge in the CBD in up to 20-25% of cases (2,3). It is unclear whether the detection of bile duct sludge at EUS should lead to therapeutic ERC in all cases or that a watchful waiting strategy can be adopted.

Aims & Methods: The objective of this study was to establish interobserver agreement among endosonographers regarding: 1. presence or absence of CBD stones, microlithiasis and sludge, and 2. the need for subsequent treatment.

30 EUS film fragments of patients with an intermediate probability of CBD stones were evaluated by 41 endosonographers. Experience in both EUS and ERCP, and the endosonographers' type of practice (tertiary care/ community hospital) were recorded. Fleiss' kappa statistics were used to quantify agreement between raters. Associations between levels of experience and both EUS ratings and treatment decisions were investigated using mixed effects models.

Results: A total of 1230 ratings (41 x 30 film fragments) and 1230 treatment decisions were evaluated. The overall interobserver agreement on EUS findings was fair (Fleiss' kappa 0.32). The agreement on presence or absence of stones was moderate (both κ 0.46). For microlithiasis the agreement was fair (κ 0.25) and for sludge it was poor (κ 0.16). In cases with CBD stones or with a "clean" CBD there was perfect agreement for the decision to subsequently perform an ERCP or not. In cases of microlithiasis and sludge ERC + endoscopic sphincterotomy (ES) was chosen in 78% and 51% respectively. Differences in experience in both EUS and/or ERCP and in type of practice were not significantly related to agreement on both EUS findings and/or the decision for subsequent treatment.

Conclusion: Endosonographers do not agree on the presence and subsequent need for treatment of bile duct sludge (poor agreement, Fleiss' kappa 0.16).

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Disclosure: Nothing to disclose

P1366

DIAGNOSTIC UTILITY OF LINEAR ENDOSONOGRAPHY IN PATIENTS WITH UNDETERMINED BILIARY OBSTRUCTION

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Introduction: Undetermined cause of Biliary dilatation frequently represents a diagnostic dilemma even after extensive radiological evaluation. Linear endosonography achieves high-resolution images of the bile duct, pancreas, and ampulla with more advantage to biopsy any suspected lesions.

Aims & Methods: Aim: Evaluate the diagnostic utility of endosonography for cases with undetermined biliary obstruction after inconclusive MRCP.

Patients and methods: This is a prospective, single-center clinical study carried out between Aug 2018 and Jan 2020 at specialized medical hospital, Mansoura University. Included patients presented with features of biliary obstruction (Dilated CBD > 7 mm by trans-abdominal ultrasound (TAU)) with no obvious etiology with or inconclusive MRCP. EUS was carried out using linear echoendoscope. Results of EUS were compared to the final diagnosis achieved by ERCP, cholangioscopy, pathological examination after biopsy or surgery, or follow up for 6 months at least.

Results: Forty-one patients were enrolled (22 female, mean age 55.6 ys). All patients had dilated CBD by TAU and MRCP with no sharp detected etiology (negative in 30 patients and inconclusive filling defect or biliary

stricture in 11 patients). Final diagnosis included 10 patients with pancreatic head adenocarcinoma (24.4%), 7 with ampullary adenocarcinoma (17.1%), 7 with benign distal CBD inflammation (17.1%), 6 with cholelithiasis (14.6%), 3 with duodenal diverticulum compressing distal CBD (Lemmel syndrome) (7.3%), 3 with pancreatic head neuroendocrine tumor (NET) (7.3%), two normal cases (4.9%) and the remaining three cases were cholangiocarcinoma, portal biliopathy and chronic pancreatitis. The sensitivity, specificity, PPV, NPV and accuracy of EUS in delineating the etiological diagnosis were 94.9% (37/39), 100% (2/2), 100% (37/37), 50.0% (2/4) and 95.12% (39/41) respectively.

EUS has failed to diagnose two cases with benign distal CBD inflammatory stricture. In the 30 cases with negative MRCP; EUS has succeeded to detect neoplastic causes as pancreatic head adenocarcinoma in 8 patients (26.7%), ampullary adenocarcinoma in 5 (16.7%), NET in 2 (6.7%) and benign conditions as benign distal CBD inflammation in 6 (20%), cholelithiasis in 4 (13.3), Lemmel syndrome in 3 and single case of chronic pancreatitis. Only one case has negative findings with normal final diagnosis. Fine needle aspiration or biopsy (FNB) has achieved definite pathological diagnosis in (53.7%) of total cases.

Conclusion: Linear endosonography appears to have a high accuracy in diagnosis the cause of undetermined biliary dilatation by MRCP, with higher sensitivity for small pancreatic and ampullary lesion and small stones moreover it provides the ability of tissue acquisition if needed.

Disclosure: Nothing to disclose

P1367 WITHDRAWN

P1368 WITHDRAWN

P1369

ELASTOGRAPHY GUIDED FINE NEEDLE VERSUS STANDARD FINE NEEDLE ASPIRATION IN SOLID PANCREATIC LESIONS: A PROSPECTIVE STUDY

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Introduction: The use of elastography in endosonography (E-EUS) measures the hardness of tissue by using the pattern, the strain ratio or the strain histogram. Also, E-EUS can target EUS-FNA (E-EUS-FNA) in the hardest region which correspond to the stroma rich part of the lesion. This might improve the diagnostic rate of EUS-FNA, but their superiority was not proved in any prospective study.

Aims & Methods: **Aim:** To assess if the E-EUS-FNA is superior to standard EUS-FNA in obtaining specific diagnosis in solid pancreatic masses and the factors that can lead to different diagnostic rate.

Method: This prospective study in one tertiary medical academic center included patients with the suspicion of pancreatic solid masses on trans-abdominal ultrasound or CT scan. The first pass was done during elastography assessment into the blue homogenous part of the lesion and the second pass during the standard EUS assessment by using the 22G

standard FNA needle EUS-FNA(Expect, Boston Scientific). The visible core was collected and analysed separately. The final diagnosis was based on EUS-FNA or surgical specimen results and on following up for 12 months by imaging methods.

Results: Fifty-one patients were analysed. The mean age was 64 years old and 74% of them were male. There were 85% head and istmus pancreatic lesions, and more than 89% were stage T3 and T4. The majority of the lesions were blue homogenous on qualitative elastography assessment.

The E-EUS-FNA pass and EUS-FNA had the accuracy of diagnosis of 94% and 91% respectively (p=NS) and the global accuracy of the two passes was 95%. No difference were seen for the results related to the location, size, tumor stage, chronic pancreatitis features or biliary plastic stent.

Conclusion: The diagnostic rate of core obtained by using 22G FNA needles with standard EUS-FNA and guided E-EUS-FNA did not differ statistically.

Disclosure: Nothing to disclose

P1370

ENDOSCOPIC ULTRASOUND GUIDED MICRO BIOPSY OF LYMPHOVASCULAR VESSELS IN GASTRIC SUBMUCOSAL LAYER USING MICRO FORCEPS IN A PORCINE MODEL

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Introduction: EUS-assisted needle micro biopsy (EUS-MB) is used for internal wall evaluation of pancreatic neoplastic cystic lesions showing high sensibility and specificity. This technique has not been used for analysis of the lymphovascular vessels within the submucosal gastric layer.

Aims & Methods: **Aim:** We performed a porcine model to evaluate EUS-MB within the gastric submucosal layer and assess the lymphovascular structure.

Methods: In 5 acute pigs under general anaesthesia, we created 15 submucosal pseudotumours. A linear EUS scope was used to inject 20cc of saline solution into the gastric submucosal layer in 3 anterior locations, using a 23G needle. The locations were: middle body (IA), lower body (IIA), and antrum (IIIA). Thirteen of these 15 pseudotumours were used for submucosal EUS-MB. All data were immediately registered. Biopsies were started distally at the antrum position, followed by the lower and middle body regions. EUS-MB through the 19G needle was performed by two passes of a micro-forceps in a standard technique. Samples were placed in formalin.

Pathological specimen analysis by a trained gastric wall pathologist included: size of the tissue sample (mm), quantity of blood, histological examination with Haematoxylin and Eosin (HE), immunohistochemistry (CD31, D2-40, Desmin), presence and number of vessels, presence and number of lymphatics and presence of muscularis propria.

Results: A mean of one micro forceps per two pseudotumours was used for evaluation of the submucosal vasculature. Two passes were performed for each biopsy. Specimens were handled equally by the same operator. All pseudotumours had the same size (20mm). A total of 13 biopsies were performed (5 in IA, 4 in IIA, 4 in IIIA). In 7, the microforceps was passed through a 19G conventional needle (19G-n), and in 6 through a 19G access needle (19G-ac). Among the 13 samples, 10 were considered positive

(ok+) including tissue for interpretation, and 3 were negative (ok-), 2 with insufficient tissue and 1 without tissue. Total tissue biopsy success rate was 77% (19G-n: 100%; 19G-ac: 50%), with a complete MB sample size of 11mm. Median submucosal diameter was 0.65mm (0.1-1.2). Specimen size ranged from 0.2x0.3mm (0.06mm²) to 2x0.8 (1.6mm²). A total submucosal area of 4.18 mm² was analysed, with a median area of 0.9 mm² per sample (0.2-1.6 mm²).

None of the ok+ samples presented blood contamination. All 10 ok+ samples showed arterial and venous vessels (11-107 per biopsy; 460 in total; of which 180 (40%) included the media). The mean vascular density was 11/0.1 mm². Only 50% of ok+ samples showed lymphatics (2-8 per biopsy; 18 in total; median of 4 (2-8) lymphatics per sample). The mean lymphatic density was 0.43/0.1 mm². Results are summarized in table 1. All specific stainings showed similar correlation to human tissue except for D2-40.

Conclusion: EUS-MB is an innovative method to assess the gastric submucosal space and its vasculature. Future promising applications of this technique include assessment prior to ESD in superficial gastric cancer with suspected minimal lymphovascular infiltration.

needles	site	biopsies	mean size	OK+	OK-
19g-n	I A II A III A	2 3 2	0.21 0.31 0.33	2 3 2	0 0 0
19g-ac	I A II A III A	3 1 2	0.24 0 0.96	1 0 2	2 1 0
Total		13	2.05	10	3

[Table1]

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Disclosure: Nothing to disclose

P1371

ENDOSCOPIC ULTRASOUND-GUIDED NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY VISUALISATION OF THE GASTRIC SUBMUCOSAL LYMPHOVASCULAR STRUCTURE IN A PORCINE MODEL

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Introduction: EUS-assisted needle-based confocal laser endomicroscopy (EUS-nCLE) is an optical biopsy method validated for evaluating pancre-

atic cystic neoplasms like serous or mucinous cystadenoma. Up to now, it has never been used to assess the gastric lymphovascular architecture directly in the submucosal space.

Aim: We evaluated EUS-nCLE within the gastric submucosal space in a porcine model for the first time.

Methods: In 5 acute pigs under general anaesthesia, we created 15 submucosal pseudotumours. A linear EUS scope and a 23G needle were used to inject 20cc of saline solution into the gastric submucosal layer in 3 anterior locations: middle body (IA), lower body (IIA), and antrum (IIIA). EUS-nCLE submucosa visualisation after intravenous injection of 5cc of 10% sodium fluorescein was performed in 14 pseudotumours.

After humidification of the CLE probe with saline solutions, all probes were introduced through a saline-rinsed 19G needle (either access or ES). One pass of nCLE assessment was performed for each pseudotumour, in a distal-to-proximal approach. Video data was recorded in each procedure for subsequent analysis.

Results: Overall, 14 EUS-nCLE were performed in locations IA, IIA and IIIA. Average time of nCLE assessment was 8 min (6-14 min). Submucosal lymphovascular architecture visualization was achieved in all cases. Two experienced gastroenterologists/endoscopists assessed the data individually, and descriptions were concordant. Different patterns emerged depending on the probe position within the submucosal space. A reticular pattern (RP) was observed superficially, adjacent to the mucosal border, a crossroads pattern (CP) in the central region of the submucosa, and a longitudinal pattern (LP) in the deep submucosa near the muscularis propria border.

Near the mucosal border, the RP consisted in small vessels of honeycomb shape, with squeezed cells in one line, difficult to discriminate, in slow and steady undulating motion. Occasionally, interstitial macrophages were observed as white shining cells. Centrally, a three-dimensional architecture of superposed slightly larger vessels was observed. These CP vessels had a straighter shape with some curves and intersections. They showed a regular turbulent intravascular flow, with cells arranged in a double-lined fashion. In the deepest layer (LP), vessels were the largest, longitudinal and in rather parallel organization. Inside these, erythrocytes and neutrophils were clearly distinguishable within the fluorescein-contrasted blood, showing less turbulent, fast undulating motions. It was hard to distinguish the different subtypes of neutrophils. The lack of specific cell markers was a pitfall for more detailed cell recognition.

In a nutshell, vascular architecture varied among submucosal space localization: thinner/reticular vessels superficially, and thicker/parallel vessels deeply. Lymphatic vessels were scattered, without a clear pattern, and devoid of interior moving cells. Moreover, connective tissue showed straight fine white lines in between the lymphovascular patterns, especially in the central regions of the submucosal space.

Conclusion: EUS-nCLE enable a real-time *in vivo* assessment of the lymphovascular architecture in the gastric submucosa. Future development of specific cancer cell markers is needed for promising applications of this technique prior to endoscopic submucosal dissection (ESD) in superficial gastric cancer, when minimal lymphovascular infiltration is suspected

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Disclosure: Nothing to disclose

P1372

DIFFERENTIATION BETWEEN PANCREATIC CYSTIC LESIONS USING IMAGE PROCESSING SOFTWARE ON ENDOSCOPIC-ULTRASONOGRAPHIC (EUS) IMAGES

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Introduction: EUS is the most sophisticated imaging modality to evaluate the different types of pancreatic cystic lesions; however, distinguishing between the malignant and benign lesions still remains challenging.

Aims & Methods: Our aim was to analyze the EUS images of the pancreatic cystic lesions using an image processing software (FIJI). We specified the echogenicity of the lesions by measuring the gray value of the pixels inside the selected areas. Besides the entire lesion, its cystic and solid parts were also selected separately for assessment. Following the software analyzing process images were divided into groups (serous cystic neoplasm (SCN), non-SCN and pseudocyst) according to the cytology results of the lesions. The intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms (MCNs) were classified as non-SCN category.

Results: Total of 33 patients' EUS images (21 females, 12 males; mean age of 60.9±10.1 and 66.3±11.6 years, respectively) were assessed. Overall 73 images were processed by the software: 36 in non-SCN, 13 in SCN and 24 in the pseudocyst group. The mean gray value of the entire lesion in non-SCN group was significantly higher than in SCN group (31.7 vs 25.5; $p=0.022$). The area ratio (area of cystic part/entire lesion) in non-SCN, SCN and pseudocyst group was 42%, 55% and 70%, respectively; significantly lower in non-SCN group than in SCN and pseudocyst group ($p=0.0058$ and $p<0.0005$, respectively). The lesion density (sum of the gray values/area of the lesion) was also significantly higher in non-SCN group compared to the SCN- and pseudocyst group (4802.48/mm² vs 3865.87/mm² vs 3192.27/mm²; $p=0.022$ and $p=0.004$, respectively). No correlation was found between the cystic CEA levels and the analyzed cystic gray values.

Conclusion: The computer-aided diagnosis decision is being used increasingly due to the rapid development of the information technology. The EUS image analysis process may have a potential to be a diagnostic tool for the evaluation and differentiation of pancreatic cystic lesions.

Disclosure: Nothing to disclose

P1373

TREATMENT OF DUODENAL STENOSES BY ENDOSCOPIC ULTRASOUND GUIDED GASTROENTEROSTOMY - AN ANALYSIS OF TECHNICAL AND CLINICAL OUTCOME

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Introduction: Duodenal stenosis leading to gastric outlet obstruction (GOO) is a serious complication to both benign and malignant diseases in the upper GI-tract and is related to increased morbidity and mortality. Traditionally, GOO has been resolved with either luminal duodenal stenting or surgical gastroenteroanastomosis. Development of lumen apposing metal stents (LAMS) has added another treatment option of GOO by introducing endoscopic ultrasound (EUS)-guided gastroenterostomy (GE). The anastomosis between the stomach and the small bowel is created under EUS guidance, and ideally facilitates long-term symptom-relief with possibly less need for reinterventions.

Aims & Methods: *Primary aim:* To evaluate the rate of technical success of EUS-GE, defined as ability to place a LAMS between stomach and small bowel.

Secondary aims: To ascertain clinical success defined as ability to reestablish oral nutrients without vomiting or bloating. Adverse events (AE) were defined according to ASGE lexicon of AE, and the number of re-interventions defined as subsequent unplanned endoscopic procedures.

This was a dual center study retrospectively analyzing consecutive cases of EUS-GE between December 2016 and May 2020.

Results: Twenty-nine patients (11 females, median age 74 (range 34-96), median ASA 3 (range 2-4)) with duodenal stenosis (3 benign, 26 malignant) treated with EUS-GE were identified. The EUS-GE procedures were performed in general anaesthesia in 22 patients (76%). In twenty-two patients (76%) a 15x10mm LAMS was used, and 20x10mm LAMS in seven patients (24%). Median procedure time was 76min (range 45-195). Technical success was obtained in all patients (100%), while clinical success was obtained in 26 patients (89%). Eight patients (28%) encountered an AE. Two patients had a late moderate severity AE with migration of the stent to the peritoneum and colon, respectively. Four patients with malignant GOO had a post-procedural fatal AE; one patient developed re-feeding syndrome and secondary arrhythmia, one patient had intestinal obstruction due to a distal stenosis in the jejunum and secondary aspiration of stomach content, one patient had a bleeding from the duodenal stenosis wherefrom a malfunctioning metal stent was removed during the EUS-GE procedure, and one patient died of pneumonia. Two patients had an intra-procedural moderate severity AE due to perforation and bleeding at the LAMS site, respectively; nonetheless, both were handled endoscopically by clips. Patients were discharged after a median of 3 days ($n=25$, range 0.5-12 days). Four patients (with fatal AE) died during hospitalization within less than a week after the EUS-GE procedure. With a median follow-up period of 8 weeks (range 0.5-113), the number of re-interventions was 3, or 0.1 re-intervention per patient: two patients due to migrated stent 3 weeks after the EUS-GE procedure and one patient due to the initial perforation. The median survival was 8 weeks ($n=29$, range 0.5-113). Twenty-one patients (72%) died after median 6 weeks (range 0.5-23). Eight patients (28%) (3 with benign GOO) were still alive at median follow-up of 16 weeks (range 1-113).

Conclusion: EUS-GE is a promising treatment for GOO with an excellent technical and clinical results. However, the number and severity of AE calls for optimized pre- and postoperative work-up. Prospective randomized trials comparing luminal stent and EUS-GE are warranted to compare the techniques.

Disclosure: Nothing to disclose

P1374

ENDOSCOPIC ULTRASOUND-GUIDED RADIOFREQUENCY ABLATION OF PANCREATIC METASTASIS FROM RENAL CELL CANCER: FEASIBILITY AND SAFETY

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Introduction: Renal cell carcinoma (RCC) is the most common renal cancer in adults. Up to 50% of patients will develop metastases after nephrectomy with a 5-year survival rate of 10%-15%. Pancreas is an elective site for RCC metastases. Surgery is the first choice treatment for pancreatic metastases. For not-resectable pancreatic metastases therapeutical options are limited. Radiofrequency ablation (RFA) has been successfully performed for the treatment of several not-resectable solid tumours. Previous studies have demonstrated the feasibility and safety of endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) for the treatment of pancreatic lesions. However, there are no data regarding its use in the treatment of pancreatic metastases from RCC.

Aims & Methods: To evaluate feasibility and safety of EUS-RFA in the treatment of pancreatic metastases from RCC.

It is a single centre prospective study on patients with non-resectable RCC pancreatic metastases or not amenable to surgery. All patients underwent EUS-RFA with a monopolar, 19G RFA needle (Endoscopic UltraSound guided Radiofrequency Ablation electrode; EUSRA) with a RF power of 30W. All patients underwent CT/MRI scan after 24 hours from the procedure. Feasibility was defined as the possibility of inserting the needle in the lesion and applying the radiofrequency. Safety was defined by collecting data of any complication occurred within 3 months of follow-up.

Results: From January 2019 to January 2020, three patients were enrolled (2 women; mean age 64±19 years). Overall, four lesions were treated (Mean size 26±17mm). 3 out of 4 lesions were located in pancreatic head. The procedure resulted feasible in 100% of cases. No complications occurred after the treatment.

The post-procedural imaging showed in all cases the presence of a necrotic area in the site of treatment.

Conclusion: EUS-RFA seems to be a feasible and safe technique for the treatment of not-resectable pancreatic metastases from RCC. Further studies are necessary to determine the efficacy of this treatment.

Disclosure: Nothing to disclose

P1375

RISK FACTORS FOR BLEEDING AFTER ENDOSONOGRAPHIC (EUS)- GUIDED PUNCTURE

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Introduction: EUS-guided fine-needle aspiration/biopsy FNA/FNB) is an established technique for evaluation of gastrointestinal and pancreatic tumors and considered as a procedure with high risk for bleeding.

Aims & Methods: To compare the bleeding rate between different tumors regarding the type of tumor, type of needle, coagulation parameters, and use of antithrombotic agents.

METHODS: Our multicentric retrospective analysis included EUS-FNA/FNB of abdominal lesions performed between 01/2016-04/2020 in Klagenfurt, 11/2018-12/2019 in St. Pölten and 01/2018-12/2019 in Cottbus. EZ Shot 3 (Olympus) (19 or 22G) flexible nitinol needle, EchoTip® Ultra (Cook) (19 or 22G) and Expect™ (Boston Scientific) (19 or 22G) and were used for EUS-FNA and SharkCore™ (Medtronic) (19 or 22G) or Boston Acquire™ (Boston Scientific) (22G) were used for EUS-FNB.

Needles were chosen according to the availability in the centers and endoscopist preference.

Minor bleeding was defined as an event with a duration of more than one minute, no need for intervention, a large coagulum on the puncture site, or a decrease in hemoglobin ≥ 1.5 g/dL (but less than < 2 g/dL). Major bleeding was defined as a reduction in hemoglobin level ≥ 2 g/dL, need of a transfusion, or interventional hemostasis.

Antithrombotic agents were managed according to the ESGE guidelines. Acetylsalicylic acid was continued in almost all patients who underwent EUS-FNA/FNB, while in the patients with low thrombotic risk, P2Y12 receptor antagonists (clopidogrel) and warfarin were discontinued five days before the procedure. The last dose of DOACs (rivaroxaban, apixaban dabigatran) was taken 48 hours before any procedure.

Parameters analyzed regarding the occurrence of bleeding were: age, type of the tumor, use of antithrombotic/anticoagulant agents, platelets count, prothrombin time, and use of EUS-FNB needles.

Results: 461 EUS-FNA/FNB were assessed (Klagenfurt - 292, St. Pölten - 111 and Cottbus - 58 cases). FNA was performed in 67.8 % of cases.

EUS-FNA/FNB was performed for the following indications: solid pancreatic masses - 251 cases (54.4%), pancreatic cysts - 100 (21.7%), subepithelial gastrointestinal tumors - 58 (12.6%), abdominal lymphadenopathy - 25 (5.4%), mediastinal tumors - 19 (4.1%), liver tumors - 6 (1.3%) and other indications - 2 cases (0.4%).

One major bleeding (0.2%) occurred in our cohort (bleeding from duodenal vessel occurred after EUS-FNB of a solid pancreatic tumor), but no events with hemodynamic instability were observed.

Minor bleeding occurred in 44/461 (9.5%) of cases.

The use of FNB needles was associated with the occurrence of bleeding (Table), while tumor type, antithrombotics/anticoagulation, platelet count and prothrombin time were not associated with the risk of bleeding.

Factor	Without bleeding (n=416)	Any type of bleeding (n=45)	p-value
Age (years)	65.1±13.5	64.3±7.7	0.72
Antithrombotics/anticoagulants: -continued/discontinued/all	14.4%/11.8%/26.2%	17.8%/15.5%/33.3%	0.69/0.63/0.39
Platelets (cells/mm3)	243285±72202	230500±14489	0.57
PT (%)	96.1±10.3	95±11.3	0.63
FNB needles	28.3%	66.6%	<0.0001
Type of tumor Solid pancreatic mass/Cystic pancreatic mass/Subepithelial tumor/Other tumors	53.1%/22.3%/12.9%/11.7%	66.7%/15.5%/8.9%/8.9%	0.11/0.38/0.59/0.75

[Table]

Conclusion: The use of EUS-FNB needles increases the rate of minor bleeding, while major bleeding is a rare occurrence, irrespective of the needle type.

Disclosure: Nothing to disclose

P1376

AN ITALIAN SURVEY ON THE USE OF LUMEN-APPPOSING METAL STENTS: PRESENT AND FUTURE PERSPECTIVES

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Introduction: Endoscopic ultrasonography (EUS)-guided transluminal drainage has undergone an exponential development over time and the introduction of a new dedicated type of stent, called Lumen-Apposing Metal Stent (LAMS), has revolutionized this panorama. It is a fully-covered, barbell-shaped, metal stent with two-side flanges, characterized by anti-migratory properties allowing direct therapeutic interventions through a wide and short channel¹.

LAMS has three on-label indications: pancreatic fluid collections (PFC) drainage^{2,3}, biliary drainage (BD)⁴, for relieving biliary obstruction after failed endoscopic retrograde cholangiopancreatography (ERCP); gallbladder drainage (GBD)⁵, for treatment of acute cholecystitis in high-risk surgical patients. Among off-label indications, gastroentero-anastomosis (GE-A) for management of gastric-outlet-obstruction is the most promising⁶.

Aims & Methods: The aim of this survey is to investigate peri-procedural aspects of LAMS placement nationwide. A questionnaire, composed of 48 questions grouped under five sections (expertise, peri- and intra-procedural aspects, budget/refund, future perspectives), was submitted to Italian LAMS-users in November 2019-January 2020. Practices of more or less experienced endoscopists were compared by chi-squared test. Statistical analyses were performed using SPSS®.

Results: 36, out of 40, Italian centers performing interventional EUS and LAMS placement completed the survey. Among specialists, 42% have >15 years of endoscopic experience, 58% in all kind of interventional endoscopy (EUS, ERCP, endoluminal), 58% perform >250 EUS/year, 53% >200 ERCP/year, 61% placed overall < 20 LAMS (56% < 10/year).

1. Indications for LAMS positioning are: 97% PFCs drainage, 80% BD, 75% GBD, 20% GE-A. 78% of endoscopists perform only on-label procedures,

22% both on/off-label. Concerning the training, 39% attended a preliminary course, 28% were just supported by an expert, 22% had both the opportunities, 8% didn't do any of them.

2. Management of antiplatelets therapy is very disomogeneous. Only half of the participants discusses the case in a multidisciplinary meeting and, during follow-up, these patients are evaluated in a specialized clinic only in 30% of cases. After PFC drainage, 66% of endoscopists carry on with proton pump inhibitors therapy. Post-procedural imaging is performed by 52-70% of endoscopists only if there is a suspected adverse event, always an abdominal contrast-enhanced CT-scan by 20-43% or an abdominal ultrasonography by 6-22%.

No significant differences were found among more or less experienced endoscopists about on- vs on/off-label indications, perception of technical complexity and post-procedural imaging request (p>0.05).

3. 8% of endoscopists work in a standard endoscopic room without fluoroscopy. Sedation protocol is very different among centers.

4. Refund for LAMS is guaranteed in 28% of cases for PFCs drainage, 11% for BD and GBD, in no one region for GE-A.

5. Main future growing indications appear to be BD, GBD and GE-A (70%, 55%, 55% respectively). Most of participants consider necessary an experience in all kind of interventional endoscopic procedures for training.

Conclusion: This is the first survey assessing the state of the art on LAMS almost 10 years after their introduction in interventional EUS practice. There are currently wide variations in practice nationwide, which demonstrates a pressing need to define technical, qualitative and peri-procedural requirements to carry out this procedure, towards a standardization.

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P1377

SAFETY AND EFFICACY OF AN ENTEROSCOPY-BASED APPROACH IN REDUCING THE POLYP BURDEN IN PATIENTS WITH PEUTZ-JEGHERS SYNDROME: EXPERIENCE FROM A TERTIARY REFERRAL CENTRE

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Introduction: Patients with Peutz-Jeghers syndrome (PJS) develop hamartomatous polyps in the small-bowel (SB), possibly causing complications such as anemia, intussusception and bowel obstruction. Moreover, these patients have an increased risk of developing gastrointestinal (GI) and extra-GI cancers.

In this study we aimed to evaluate the impact of an enteroscopy-based approach on the reduction of the polyp burden in a cohort of adult PJS patients.

Aims & Methods: We conducted a retrospective study at the City of Health and Science University Hospital, Turin, Italy. We included all consecutive PJS patients (≥ 18 years old) eligible for DAE or IOE, between January 2003 and November 2019, after the detection of at least 1 SB polyp ≥ 1.5 cm during screening diagnostic procedures (e.g. capsule endoscopy, magnetic resonance enterography, CT enterography and SB series / enteroclysis). The choice between DAE (single- or double-balloon enteroscopy) and IOE was taken after multidisciplinary discussion, on a case-by-case basis.

Push enteroscopy procedures were excluded "a priori" from the analysis, in order to increase homogeneity of the results. Enteroscopy technical issues and complications were recorded. At the time of index enteroscopy the patients' clinical records were retrospectively reviewed, and clinical data were recorded until November 2019.

Results: Overall, 24 adult patients were included. 15 (62.5%) were male, the median age was 33.5 years (IQR: 25-43.5). Before inclusion in the study, 16/24 patients (66.7%) had already undergone SB surgery for polyp-related complications, 13 of which (13/16, 81.2%) in an emergent setting. Two patients (2/24, 8.3%) had a positive history for SB adenocarcinoma, which was treated surgically in an elective setting. During the study timeframe, 47 DAE and 9 IOE were performed and 247 SB polyps were endoscopically removed (size range 5-60 mm). 181 of these polyps (73.3%) measured ≥ 15 mm. 158/247 polyps (64.0%) were resected during DAE (median number of polyp per DAE: 2.0, IQR 1.0-4.0) and 89 (36.0%) during 8 IOE (median number of polyp per IOE: 7.5, IQR 6.0-17.0).

242 out of 247 polyps were histologically confirmed as hamartomas, 1 was a tubulo-villous adenoma with high-grade dysplasia and 1 was a serrated polyp with low-grade dysplasia; 3 polyps were not retrieved after resection.

To note, there was a stable increase of DAE procedures over the years, whereas IOE decreased progressively. The overall rate of procedural complications was 12.8% (8.5% for DAE, 22.2% for IOE); of note, the only perforation in our series was directly related to enterotomy, after IOE.

The median observation time was 108 months (IQR 35.5-163.7): in this timeframe 2 patients developed SB polyp-related complications requiring emergent surgery. No SB neoplasms were reported whereas in 8/22 patients (36.4%) 9 extra-GI neoplasms were recorded. Three patients died during the observation period: all deaths were related to extra-GI neoplasms.

Conclusion: Results of our study show that the enteroscopy-based approach appears to be effective in decreasing polyp-related complications in PJS patients, thus reducing the need for emergent surgery. The rate of procedural complications is acceptable, especially in DAE procedures.

Although the prevention of SB polyp-related complications remains the main goal of screening programs, the high incidence of extra-GI neoplasms appears to be a rising issue in the management of these patients.

Disclosure: Nothing to disclose

P1378

ROLE OF VIDEOCAPSULE AND DOUBLE BALLOON ENTEROSCOPY IN PATIENTS WITH INDICATION OTHER THAN SUSPECTED SMALL BOWEL BLEEDING

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Introduction: The use of enteroscopic procedures, videocapsule and double balloon enteroscopy (VCE, DBE), in patients with indications other than suspected small bowel bleeding (SSBB) is largely unknown and in literature there are no evidences on this issue.

Aims & Methods: Our aim has been to assess the clinical impact of VCE/DBE in patients without SSBB as main indication.

We retrospectively evaluated consecutive patients underwent VCE and/or DBE from March 2001 to January 2019. Patients without SSBB (NSSBB) as indication were considered. Demographic and clinical parameters of the patients, technical characteristics of the procedures and adverse events were collected. Effectiveness of VCE and DBE in terms of diagnostic yield (DY), concordance between the two investigations (VCE and DBE), final diagnosis, and safety of the procedures were evaluated.

Results: 1168 VCE and 607 DBE were collected (1366 subjects). 530(45%) VCE and 290(47%) DBE were performed for NSSBB (615 patients, 62% females, 48 $\pm$ 16 years of age). Main indications were: suspected or known Crohn's disease, complicated celiac disease, persistent enteric symptoms, suspected neoplasms, other (polyposis syndromes, enteropathy, lymphangiectasia). No technical differences have been noted between VCE and DBE performed for NSSBB or SSBB. Compared to SSBB, the NSSBB group presented a significantly higher prevalence of females (63% vs 53%) and younger age (48 vs 66 years). The DYs were 64% vs 58% ($p < .05$) and 52% vs 69% ($p < .05$) for VCE and DBE, NSSBB vs SSBB. The lowest DY (35%) has been found in case of DBE performed for suspected tumors. The rate of adverse events was 0% in VCE and 0.7% in DBE without differences between NSSBB and SSBB. In patients performing both VCE and DBE, the agreement was sub-optimal ($k = 0.13$); however, it was very variable depending on the different indications, being higher in celiac disease ($k=0.7$) and in Crohn's disease ($k=0.6$), and lower in suspected neoplasms ($k=0.07$) and in persistent enteric symptoms ($k=0.25$).

Conclusion: In this study we have collected the largest series of patients undergoing VCE and DBE for indications other than bleeding. Compared to classical indications, the DY of enteroscopies in case NSSBB is good and in some cases better than that of SSBB with a similar safety profile. The study demonstrates the efficacy of enteroscopy also in case of "atypical" indications.

Disclosure: Nothing to disclose

P1379

CLINICAL IMPACT OF VIDEOCAPSULE AND DOUBLE-BALLOON ENTEROSCOPY IN SUSPECTED SMALL BOWEL BLEEDING: RESULTS FROM A 18 YEARS-LONG EXPERIENCE

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Introduction: Suspected small bowel bleeding (SSBB) is the main indication for videocapsule and double balloon enteroscopy (VCE, DBE). SSBB studies are characterized by a reduced sample size, mainly involving eastern countries and rarely including both data from VCE and DBE.

Aims & Methods: We assessed in a large cohort of SSBB patients the impact of VCE and DBE, in terms of diagnostic yield, concordance and follow-up.

We retrospectively evaluated consecutive patients with SSBB who underwent VCE and/or DBE from March 2001 to January 2019. Demographic and clinical parameters of the patients, technical characteristics of the procedures and adverse events were collected. We assessed effectiveness of VCE and DBE in terms of diagnostic yield (DY), concordance between the two investigations (VCE and DBE), hemoglobin values before and after DBE (and after a 12 months follow-up), and safety of the procedures.

Results: Overall, 1366 patients (1168 VCE/607 DBE) were analyzed. 751(55%) patients underwent VCE and/or DBE for SSBB and specifically 638 VCE and 317 DBE (226 anterograde) have been performed. In SSBB population, the DY was 58.3% and 69.4% for VCE and DBE, respectively. The highest DY (76.6%) was found in case of patients undergoing DBE for overt active bleeding. For both VCE and DBE, the DY was significantly higher in patients over 65 years of age. The DY of VCE is significantly higher in overt bleedings compared to occult ones (65.2% vs 56.3%; OR 1.455, IC95% 1.025-2.147) and amongst occult ones the DY is higher in case of age > 65 years (61.4% vs 51%; OR 1.527, IC95% 1.068-2.183). Regarding DBE, no significant differences were found between overt and occult bleeding. Most frequent detected lesions were: angiectasia (50%), tumors (10%), ulcers (10%), and stenosis (3%).

Concordance between VCE and DBE was generally suboptimal (k=0.2); however, concordance was greatly influenced by the time interval between the two procedures, being good (k=0.55) in case of a 3-5 days interval.

The post-procedural mean hemoglobin values are significantly higher than the pre-enteroscopy values, even up to 12 months of follow-up (8.92 ± 1.69 g/dl 1 month before DBE, 10.55 ± 2.09 g/dl 12 months after DBE; p < 0.0001).

No capsular retentions have been recorded. In case of DBE, 6 (0.9%) mild adverse events and 59 cases (31.6%) of isolated hyperamylasemia were noted.

Conclusion: The study describes the broadest European monocentric cohort. VCE and DBE play a pivotal role in the diagnostic-therapeutic approach of SSBB. Concordance between VCE and DBE demonstrated the importance of performing these procedures as soon as possible. The clinical impact is high in elderly patients and maintained also during follow-up.

Disclosure: Nothing to disclose

P1380

MOTORIZED SPIRAL ENTEROSCOPY-ASSISTED ERCP IN ALTERED GASTROINTESTINAL ANATOMY: FIRST CLINICAL SERIES

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Introduction: Recently novel motorized spiral enteroscopy (MSE) has been introduced into clinical practice and has been shown to be safe and effective for antegrade deep enteroscopy in patients without previous abdominal surgery [1]. MSE has not yet been studied in patients with surgically altered anatomy of the upper gastrointestinal tract. ERCP in this group of patients often needs device assisted enteroscopy, in particular after Roux-en-Y reconstructive surgery. Balloon guided- or manual spiral enteroscopy are well established for these indications but they are often time-consuming and technically challenging. We recently reported the first case of motorized spiral enteroscopy for ERCP in a patient after Roux-en-Y reconstructive surgery [2].

Aims & Methods: All patients undergoing MSE-assisted ERCP after Roux-en-Y reconstructive surgery were retrospectively analyzed at a tertiary reference center since 2016 to evaluate feasibility, success- and adverse event rates of MSE-assisted ERCP.

Results: Overall, ten patients (5 female, 5 male) with a median age of 71 years (range 52-87) could be identified. All patients had co-morbidities (ASA II 20%, ASA III 80%). Indications for ERCP included biliary strictures (n=5), biliary stones (n=3) and others (n=2). All patients had a Roux-en-Y-anatomy. Technical success rate of MSE (reaching the papilla or bilio-enteric anastomosis) was 80% (8/10). Overall success rate of ERCP (successful cannulation with obtaining a cholangiogram) was 87.5% (7/8) with 75% (3/4) for a normal biliary anatomy and 100% (4/4) for biliodigestive anastomosis. After biliary cannulation, therapeutic interventions were successfully performed in all patients including balloon-dilation (n=7), stone extraction (n=2), stenting (n=2) including one implantation of a self-expandable metal stent, needle-knife precut-sphincterotomy (n=1), tissue acquisition from stricture (n=1) and stent extraction (n=1). Median total procedure time was 70 minutes (range 42-165). Adverse event rate was 10% (self-limiting prolonged bleeding after balloon dilatation of the bilio-enteric anastomosis in one patient). No serious adverse events were registered.

Conclusion: The current series showed for the first time the feasibility of motorized spiral enteroscopy for ERCP in patients with surgically altered upper gastrointestinal anatomy. The results indicate that biliary access and therapeutic interventions can be achieved in most of the cases with a low rate of adverse events. These data justify further evaluation of this new technique preferably in a prospective multicenter trial.

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P1381

AUTOMATED GRADING OF ULCER SEVERITY ON VIDEO-CAPSULE IMAGES OF CROHN'S DISEASE WITH CONVOLUTIONAL NEURAL NETWORKS

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Introduction: Capsule endoscopy (CE) is a prime modality for Crohn's disease (CD) diagnosis and follow-up. Endoscopic severity of the ulcers is of much importance for CD course. Deep learning has been proven to be accurate in detection of ulcers on CE. However, to date, endoscopic classification of the ulcers by deep learning has not been attempted. The aim of our study was to develop a deep learning algorithm for the automated grading of CD ulcers on CE.

Aims & Methods: We retrospectively collected CE images of CD ulcers from our CE database. Each ulcer severity was graded by two capsule readers based on Pillcam CD classification and the inter reader variability was analyzed. Then, a consensus reading by 3 capsule readers was done. The consensus reading was used to train and test an ordinal convolutional neural network (ordinal CNN) to automatically grade images of ulcers. A pre-training stage included training the network on images of normal mucosa and ulcerated mucosa. Then, five-fold cross validation was performed for training and testing the network's ability to grade the severity of ulcers.

Results: Overall, our dataset included 17,640 CE images from 49 patients; 7391 images with mucosal ulcers and 10,249 normal images. 1108 randomly picked pathological images were further graded from 1-3 according to the ulcer severity (488 /436/184, respectively). Pre-training was performed using the normal mucosa vs. ulcerated mucosa images.

For the graded images, the network achieved classification accuracy of 0.91 (CI 0.867 - 0.954) for grade 1 vs. grade 3, 0.78 (CI 0.716-0.844) for 2 vs. 3 and 0.624 (CI 0.547-0.701) for 1 vs. 2.

Conclusion: CNN achieved high accuracy in detection of severe CD ulcerations. CNN-assisted CE reading in CD patients can potentially facilitate and improve monitoring and diagnosis in these patients.

Disclosure: Nothing to disclose

P1382

A NOVEL CAPSULE ENDOSCOPE WITH MULTIPLE CHROMIC SENSORS

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Introduction: Capsule endoscopy is a non-invasive visual modality for investigating the GI tract. Several capsule endoscopic devices have been proposed for examining functions or treating gastrointestinal (GI) diseases such as pH, secretions and drug delivery. We propose a novel capsule endoscope with multiple chromic sensors (CECS) that do not consume any energy. It may be possible to not only use the CECS to evaluate GI functions and the gut's microbiome, but also to diagnose lesions on site.

Aims & Methods: The novel CECS was composed of a conventional capsule endoscope and chromic sensors attached to its outer sheath. In the first trial, the CECS was equipped with the tape sensors used in urinalysis (pH, glucose, protein, hemoglobin, ketones) and a urease test for Helicobacter pylori. Changes in their color appeared around the edges of the endoscopic images. To decide the optimal size and position for the chromic

sensors, the capsule's field of view and the visibility of color changes on the images were evaluated by changing the size of the sensors and attaching them in different positions. After that, I evaluated how long the color change continued for and whether the chemical reaction was reversible or not.

Results: 1) The sensors reduced the field of view by ten degrees (172 to 162) partially because they protruded slightly over the optical dome. 2) The precision of the pH sensor was within 7%, glucose was within 50mg/dl and occult blood was within 5 red cells / μ l. 3) Adhesive tape over the reagents enabled the sensors to function for 3 hours minimally because it prevented the reagents from being washed away. 4) The test strip for the urease test could validate whether Helicobacter pylori was present or not in the stomach of the phantom.

Conclusion: The results suggest that it may be possible to use chromic sensors on a capsule endoscope to detect bleeding points precisely, bacteria and enzyme function.

Disclosure: Nothing to disclose

P1383

NATURAL LANGUAGE PROCESSING DRIVEN COMPARISON OF SMALL BOWEL MRI AND CAPSULE ENDOSCOPY REPORTING FOR CROHN'S

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Introduction: Small Bowel Capsule Endoscopy (SBCE) has an established role in the diagnosis/management of small bowel Crohn's disease (CD). Previous work has suggested its diagnostic yield is comparable to that of Small Bowel MRI (SBMR), but the narrative nature of reporting makes this challenging to evaluate formally.

Aims & Methods: Anonymised data from the electronic health record were systematically extracted from patients undergoing SBCE at our hospital between Jan 2016- Jan 2020 and categorised according to indication. A subgroup with suspected or established Crohn's disease was identified, and corresponding SBMR and calprotectin results were obtained. Natural language processing (NLP) techniques were used to compare the content and diagnostic accuracy of the reports.

Results: Out of 1016 patients undergoing SBCE, 494 patients were suspected as having small bowel CD. Of this cohort, 133 underwent SBCE within 180 days of SBMR. 59 patients had corresponding faecal calprotectin (FC) measured (Mean: 318.12+/-138.39).

Tokenisation (splitting sentences into smaller units for analysis) demonstrated that the style and content of the SBCE vs SBMR reports were very different in form and structure. The resultant 'word-bags' (counts/weightings of individual words) revealed that SBCE reports had significantly more 'diagnostic' weight, as described in Table 1.

Small Bowel Test	'Crohn's' mentioned as the potential diagnosis	A positive finding of small bowel 'inflammation / ulceration' described	A positive finding of a 'stricture' described	Terms of uncertainty used in report conclusion	A positive finding of 'thickening' described
SBMR	3.75% (n=5)	6.02% (n=8)	3.01% (n=4)	11.28% (n=15)	6.77% (n=9)
SBCE	14.29% (n=19)	17.29% (n=23)	3.76% (n=5)	2.26% (n=3)	0.75% (n=1)
X2 & p-value	8.98 (p=0.003)	8.22 (p=0.004)	0.12 (p=0.115)	8.58 (p=0.003)	6.65 (p=0.009)

[Table 1: SBMR / SBCE diagnostic characteristics (X2 = Chi-Squared Statistic)]

Mean FC was significantly higher in patients with the term 'ulceration' reported on SBCE (703.5+/-353) compared to 'no ulceration' (265.2+/-148.38) ($p=0.044$) linking the word 'ulceration' with more severe disease descriptions.

Conclusion: NLP is a powerful novel tool to compare narrative diagnostic accuracy between SBCE and SBMR not previously described. FC is positively correlated with small bowel 'ulceration' linking descriptive, diagnostic terms to biomarkers. According to our results, SBCE alone rather than SBMR is necessary to investigate small bowel Crohn's disease unless full-thickness stricturing is suspected from clinical symptoms.

Disclosure: Nothing to disclose

P1384

PREDICTING AN INADEQUATE COLON CAPSULE CLEANSING: A STUDY APPROACHING PREDICTIVE FACTORS

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Introduction: The colon capsule may be valuable in the approach of several colon pathologies. An adequate colon cleansing is paramount to rely on reported findings. To optimize the rate of adequate cleansing it may be important to identify risk factors that can predict an sub-optimal colon preparation. Being able to properly categorize the patients at major risk, will allow to select the subgroup in most need of enhanced cleansing protocols.

Aims & Methods: **Aim:** To define predictive factors for inadequate bowel preparation in colon capsule.

Methods: Retrospective, single center, cohort study. Patients' demographics and data including endoscopic findings and quality of bowel preparation assessment were collected retrospectively from the medical records. A univariate analysis tested the association between covariables and the outcome, inadequate cleansing. The statistically significant variables were included in multivariable logistic binary regression.

Results: We included 83 consecutive colon capsules, from 2015 to 2019. Seventy-seven percent were female, with a mean age of 65 years. The main indication for initial colonoscopy was colorectal cancer screening (44%) followed by polyp surveillance (25,3%). The major reason for incomplete conventional colonoscopy was fixed angulation of the left colon (63%). Fifty percent of the colon capsules cleansing was graded as inadequate. The variables colonic transit time, previous inadequate preparation, impaired mobility, polymedication, chronic antidepressants, calcium channel blockers, chronic laxative drugs, obstipation and multiple comorbidities were statistically associated with an inadequate cleansing ($p < 0.05$). The variables previous inadequate cleansing (OR 8.3; $p = 0.032$), chronic laxative (OR 13; $p=0.026$) and chronic antidepressant medication (OR 12; $p = 0.018$), were independently associated with the outcome inadequate cleansing.

Conclusion: Previous inadequate cleansing, chronic laxative and chronic antidepressant medication may increase the rate of inadequate colon capsule cleansing up to 13-fold risk. These factors seem essential in the selection of patients for optimization of the colon cleansing protocol, aiming to diminish the rate of inadequate colon capsule cleansing.

Disclosure: Nothing to disclose

P1385

CAPSULE ENDOSCOPY IN QUIESCENT SMALL-BOWEL CROHN'S DISEASE: IS MUCOSAL HEALING ALONE A RELIABLE INDICATOR OF A FLARE-FREE DISEASE?

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Introduction: Small bowel capsule endoscopy (SBCE) may play an important role on established small bowel Crohn's Disease (CD), if deemed to influence patient's management. However, optimal monitoring strategies for predicting disease course remain uncertain. Mucosal healing has been proposed as a valuable indicator of a flare-free disease.

Aims & Methods: Our aim was to evaluate the occurrence of disease flare on patients with quiescent small bowel CD and mucosal healing on SBCE, as well as to test possible features identifying patients with a higher risk of having such disease course.

We conducted a retrospective single center study of consecutive patients with quiescent small bowel's CD - L1 ileal disease according to the Montreal classification - submitted to surveillance SBCE. Only patients with mucosal healing on SBCE (Lewis Score < 135) were considered, with a minimum follow-up of 12 months being required after SBCE. Forty-seven patients were included between January 2011 and March 2019. Disease flare (defined as the need for treatment change or intensification, hospitalization or bowel resection) during the follow-up period was assessed. Different patient- and disease- related variables were analyzed as possible predictors of disease flare in this set of patients. Statistical analysis was performed using SPSS statistics v23.0.

Results: Of 47 patients with mucosal healing at baseline, 12 (25.5%) had a flare during the 12-month follow-up. The median time of flare onset was 6 months after SBCE. There was 1 case of hospitalization due to bowel obstruction unrelated to the procedure. Age ≤ 30 years ($p=0.048$), extra-intestinal manifestations ($p=0.033$) and platelets count $\geq 280 \times 10^9/L$ ($p=0.045$) were on multivariate analysis significantly associated with CD flare on the first year after achieving mucosal healing.

Conclusion: Patients with quiescent CD and mucosal healing are still not free of the risk of disease flare on the first year after index SBCE. Factors such as younger age, extra-intestinal manifestations and thrombocytosis were in our series associated with increased risk of CD flare. These may be helpful on selecting patients in need of an earlier clinical or endoscopic reevaluation.

Disclosure: Nothing to disclose

P1386 WITHDRAWN

P1387

PREDICTORS OF GASTROINTESTINAL TRANSIT TIMES OF COLON CAPSULE ENDOSCOPY

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Introduction: In order for Colon Capsule Endoscopy (CCE) to obtain images of the entire gastrointestinal (GI) tract, the optimal transit time has to be fast enough to achieve completion within the battery time but not so fast that lesions may be missed.

Aims & Methods: We aimed to identify predictors for CCE transit times in a prospective cohort. Healthy participants received CCE with corresponding bowel preparation (5mg bisacodyl, 2L polyethylene glycol (PEG) and 2L water, both split-dose) and booster regimen (10mg metoclopramide (if capsule remained in stomach > 1 hour) and 0,5L oral sulfate solution (OSS) split dose). Possible transit time predictors were obtained through questionnaires and included age, gender, body mass index (BMI), smoking status, coffee intake, fiber intake, diet quality, physical activity, dyspeptic complaints, changed stool pattern, history of abdominal surgery, medication use and CCE findings. Multivariate logistic and linear regressions with backward elimination were performed to predict CCE completion rate and stomach-, small bowel (SB)-, colonic- and total transit times.

Results: A total of 451 CCE procedures were analyzed. Completion rate was 51.9%. Median CCE transit time was 55 minutes (IQR 40-92) for the stomach, 47 minutes (IQR 29-78) for SB and 392 minutes (IQR 191-528) for the colon. Significant predictors for a slower transit time in stomach and SB were a lower BMI ($\beta=0.131$, $p=0.017$), and lower physical activity ($\beta=0.124$, $p=0.038$) and no need to use the prescribed metoclopramide (capsule in stomach < 1 hour) ($\beta=0.165$, $p=0.005$) respectively. Significant predictors for a slower colonic transit were a lower BMI ($\beta=0.118$, $p=0.031$), higher fiber intake ($\beta=0.143$, $p=0.009$) and history of abdominal surgery ($\beta=0.180$, $p=0.001$). Significant predictors for a slower total GI transit time were a lower BMI ($\beta=0.129$, $p=0.035$), an unchanged stool pattern ($\beta=0.125$, $p=0.039$) and history of abdominal surgery ($\beta=0.145$, $p=0.017$). Unchanged stool pattern (OR 0.309, 95% CI 0.125-0.763, $p=0.011$) and history of abdominal surgery (OR 0.458, 95% CI 0.271-0.775, $p=0.004$) also resulted in a lower completion rate.

Conclusion: Lower BMI, lower physical activity, fiber intake, unchanged stool pattern and history of abdominal surgery were significant predictors for slower CCE transit times. In future practice, these factors can be used to anticipate a longer capsule transit time and possibly intensify the preparation protocol. The faster SB transit in participants who took metoclopramide due to a long stomach transit, suggests that it might be beneficial to use metoclopramide in all CCE procedures.

Disclosure: Nothing to disclose

P1388

IS EXTENDED SMALL BOWEL TRANSIT TIME ON CAPSULE ENDOSCOPY ASSOCIATED WITH A HIGHER DEGREE OF INFLAMMATION IN CROHN'S DISEASE?

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Introduction: The Lewis score (LS), an endoscopic score that evaluates the inflammatory activity for small bowel capsule endoscopy (CE) in Crohn's disease (CD), depends on adequate visualization of the intestinal mucosa. It remains controversial whether a longer small bowel transit time (SBTT) may be associated with a higher diagnostic accuracy of significant lesions.

Aims & Methods: To evaluate the association between SBTT and inflammatory activity expressed by LS in patients with established CD as well as describe the association between demographic, clinical and analytical variables and SBTT in this population.

Retrospective single-centre study including consecutive adult patients undergoing small bowel CE for established CD between January 2016 and January 2020. Patients' demographic (age, sex), clinical (elapsed time between CD diagnosis and CE, bowel cleanliness, CD phenotype, LS, therapeutic regimen) and analytical data (haemoglobin, platelet count, erythrocyte sedimentation rate, C-reactive protein, faecal calprotectin (FC)) at the time of CE were recorded. Patients with insufficient data, incomplete CE, need for CE placement by endoscopy or capsule panendoscopy were excluded. SBTT was defined as the time elapsed between the first duodenal image and the first caecal image.

Results: We included 156 consecutive patients with small bowel CD submitted to CE; most were female (64.7%) with a mean age of 35±12 years. Mean SBTT was 267±102 minutes, median LS was 433 (interquartile range: 1125), with 85.3% of patients having significant inflammatory activity (LS ≥ 135). There was a positive, although weak, correlation between SBTT and LS ($\rho=0.163$; $P=0.042$) and FC ($\rho=0.274$, $P=0.012$). No statistically significant associations were observed between SBTT and other clinical, analytical and demographic variables.

Conclusion: Longer SBTT in CE is associated with higher inflammatory activity in the small bowel of patients with CD, expressed by higher values of LS and FC.

Disclosure: Nothing to disclose

P1389

SMALL BOWEL CAPSULE ENDOSCOPY IN PATIENTS WITH ALTERED GASTRIC ANATOMY: RESULTS FROM A EUROPEAN MULTICENTRE STUDY

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Introduction: Little is known about the feasibility, the technical limitations and the diagnostic yield of small bowel (SB) capsule endoscopy (CE) in patients with altered anatomy. Some practitioners consider that a past history of major gastric surgery contra-indicates SB-CE, or calls for endoscopic placement of the CE device into the duodenum.

Aims & Methods: The aim of this study was to evaluate the feasibility, the diagnostic yield, and the therapeutic impact of SB-CE in patients with gastric altered anatomy.

23 European centers were asked to retrospectively identify patients with altered gastric anatomy who had had SB-CE per oral route. Patients with a history of total or partial gastrectomy, Whipple procedure, sleeve gastrectomy, or by-pass gastric surgery, were included. Patients with endoscopic placement of SB-CE were excluded.

The primary outcome of the study was the diagnostic yield of SB-CE defined as the proportion of patients with a P1 or P2 finding according to Saurin et al. (1). Secondary outcomes were gastric and SB transit times, completion rate, cleanliness rate according to the Brotz et al. (2), complication rate, and therapeutic impact.

Results: 227 procedures from 222 patients were included in the study (123 male patients, age 62.0 ± 13.6 years). A history of partial gastrectomy was found in 51.4% cases, of total gastrectomy in 5.9%, of Whipple procedure in 10.4%, of sleeve gastrectomy in 6.0%, of gastric by-pass surgery in 6.0%, of pyloroduodenectomy in 0.5%. OGIB was the most frequent indication of SB-CE (195 examinations, 85.9%), being overt in 84 patients (37.8%) and occult in 111 patients (87.8%).

SB completion rate was 84.1%. No CE retention in the remnant upper GI tract was observed (0.0%). Complication rate was 0.0%. An asymptomatic SB retention was seen in 1 patient (0.4%) upstream an ileocaecal anastomosis for Crohn's disease, with successful endoscopic retrieval. Median [IQR] SB transit time was 287 min [237;290]. Cleanliness was rated adequate in 94.8% patients (34 missing data). In the 213 SBCE performed in 199 patients for whom gastrectomy was not total, median [IQR] gastric and SB transit times were 2 min [1;20] and 281 min [236;387], respectively. After exclusion of lesions found at the upper GI anastomotic site, the diagnostic yield for SB P1 or P2 lesions was calculated to be 44.5%. Active bleeding was seen in 7 patients (3.1%). Overall, SBCE had a therapeutic impact in 75 patients (33.0%).

Conclusion: SB-CE per oral route is feasible in patients with altered gastric anatomy, and is associated with high a completion rate, a high cleanliness rate, a low complication rate. Diagnostic yield and therapeutic impacts are similar to what seen in the literature in patients with normal gastric anatomy. Although non-comparative, these data suggest that indications for endoscopic placement of SB-CE should be limited in patients with altered gastric anatomy.

Completion	191 (84.1%)
Gastric retention at day 15	0 (0.0%)
SB retention rate at day 15	1 (0.4%)
SB occlusion rate at day 15	0 (0.0%)
Intervention for SBCE retrieval	1 (0.4%)
Stomach transit time, in patients for whom gastrectomy was not total, median [IQR]	2 [1;20] minutes
SB transit time, median [IQR]	287 [237;390] minutes
Adequate SB cleanliness overall assessment	183/193 (94.8%)
Relevance of findings	
P1	43 (18.9%)
P2	58 (25.6%)
P1 or P2	101 (44.5%)
Therapeutic impact	75 (33.0%)

[Performances of SB-CE in patients with altered gastric anatomy]

References: 1. Saurin JC, et al. Endoscopy 2003; 35: 576-584 2. Brotz C, et al. Gastrointest Endosc 2009; 69: 262-270

Disclosure: Romain Leenhardt is cofounder and shareholder of Augmented Endoscopy, and has given lectures for Abbvie. Xavier Dray is cofounder and shareholder of Augmented Endoscopy and has acted as a consultant for Alfasigma; Bouchara Recordati; Boston Scientific, Fujifilm, Medtronic, and Pentax. Deirdre McNamara has received research support / grants from Abbvie and Medtronic and consultant fees from Takeda and MSD.

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A GUIDE FOR ASSESSING THE CLINICAL RELEVANCE OF FINDINGS IN SMALL BOWEL CAPSULE ENDOSCOPY: ANALYSIS OF 8064 ANSWERS OF INTERNATIONAL EXPERTS TO AN ILLUSTRATED SCRIPT QUESTIONNAIRE

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Introduction: Although recommended, the P-score used for assessing the pertinence / relevance of findings seen in small bowel (SB) capsule endoscopy (CE) is based on a low level of knowledge (1).

Aims & Methods: The aim of this study was to evaluate the clinical relevance of the most frequent SBCE findings through an illustrated script questionnaire.

Sixteen types of SBCE findings were illustrated four times each in three different settings (occult and overt obscure gastrointestinal bleeding (OGIB) and suspected Crohn's disease (CD)), and with a variable number (n=1/ n=2-5/n≥6), thus providing a questionnaire with 192 scenarios and 576 illustrated questions. Fifteen international experts were asked to rate the finding's relevance for each question as very unlikely (-2) / unlikely (-1) / doubtful (0) / likely (+1) / very likely (+2). The median score (≤-0.75, between -0.75 and 0.75, or ≥0.75) obtained for each scenario determined a low (P0), intermediate (P1) or high (P2) relevance, respectively.

Results: 8064 answers were analyzed. Participation and completion rates were 93% and 100%, respectively. In overt or occult OGIB, resultant P2 findings were 'typical angiectasia', 'deep ulceration', 'stenosis', and 'blood', whatever their numbers, and 'superficial ulcerations' when multiple. While in suspected CD, consensus P2 lesions were 'deep ulceration' and 'stenosis' whatever their numbers, and 'aphthoid erosions' and 'superficial ulcerations' when multiple.

Conclusion: This study establishes a guide for the evaluation of relevance of SBCE findings. It represents a step forward for SB-CE interpretation and is intended to be used as a tool for teaching and academic research.

Type of finding	Found once	Found 2 to 5 times	Found 6 times or more
<i>In the setting of overt obscure gastrointestinal bleeding</i>			
Typical angiectasia	+1.00 (+0.50 ; +1.44)	+1.50 (+0.81 ; +1.75)	+1.62 (+1.06 ; +2.00)
Red spot /dot	-2.00 (-2.00 ; -1.44)	-1.75 (-2.00 ; -1.00)	-1.62 (-2.00 ; -0.75)
Diminutive angiectasia	-2.00 (-2.00 ; -1.00)	-1.00 (-1.25 ; -0.75)	-0.87 (-1.25 ; -0.06)
Aphthoid erosion	-1.62 (-2.00 ; -0.81)	-0.50 (-0.87 ; +0.19)	-0.37 (-0.94 ; -0.06)
Superficial ulceration	-0.50 (-1.44 ; +0.37)	+0.75 (+0.25 ; +1.00)	+1.00 (+0.31 ; +1.19)
Deep ulceration	+1.62 (+1.00 ; +1.94)	+2.00 (+1.37 ; +2.00)	+2.00 (+2.00 ; +2.00)
<i>In the setting of occult obscure gastrointestinal bleeding</i>			
Typical angiectasia	+0.87 (+0.5 ; +1.00)	+1.75 (+1.25 ; +2.00)	+2.00 (+1.25 ; +2.00)
Red spot /dot	-2.00 (-2.00 ; -1.37)	-2.00 (-1.75 ; -0.44)	-1.62 (-1.94 ; -0.31)
Diminutive angiectasia	-1.37 (-1.75 ; -1.00)	-0.62 (-1.44 ; -0.06)	-0.12 (-0.94 ; -0.00)
Aphthoid erosion	-1.00 (-1.75 ; -0.44)	+0.12 (+0.00 ; +0.87)	+0.62 (+0.25 ; +1.00)
Superficial ulceration	+0.00 (-0.04 ; +0.94)	+1.00 (+1.00 ; +1.44)	+1.25 (+1.00 ; +1.75)
Deep ulceration	+1.87 (+1.06 ; +2.00)	+2.00 (+1.81 ; +2.00)	+2.00 (+1.62 ; +2.00)
<i>In the setting of suspected Crohn's disease</i>			
Typical angiectasia	-2.00 (-2.00 ; -1.75)	-1.75 (-2.00 ; -1.50)	-1.87 (-2.00 ; -1.12)
Red spot /dot	-2.00 (-2.00 ; -2.00)	-2.00 (-2.00 ; -2.00)	-2.00 (-2.00 ; -1.81)
Diminutive angiectasia	-2.00 (-2.00 ; -2.00)	-2.00 (-2.00 ; -2.00)	-2.00 (-2.00 ; -1.81)
Aphthoid erosion	-0.87 (-1.19 ; -0.06)	+0.87 (+0.00 ; +1.00)	+1.00 (+0.00 ; +1.25)
Superficial ulceration	-0.12 (-0.50 ; +0.44)	+1.00 (+1.00 ; +1.25)	+1.50 (+1.06 ; +1.94)
Deep ulceration	+1.37 (+1.00 ; +2.00)	+2.00 (+2.00 ; +2.00)	+2.00 (+2.00 ; +2.00)

[Interpretation of votes (median, IQR) for various lesions in the 3 different indications of SB-CE]

References: 1. Saurin JC, et al. Endoscopy. 2003;35(7):576-84.

Disclosure: Romain Leenhardt is cofounder and shareholder of Augmented Endoscopy, and has given lectures for Abbvie Xavier Dray is cofounder and shareholder of Augmented Endoscopy and has acted as a consultant for Alfasigma; Bouchara Recordati; Boston Scientific, Fujifilm, Medtronic, and Pentax Rami Eliakim has received consultant fees from Abbvie, Takeda, Janssen and Medtronic; Research grant from Medtronic. John N Plevris has received educational support from Dr Falk, Tillots pharmaceuticals, Jinshan, and research support from Aquillant (Fujifilm). Deirdre McNamara has received research support / grants from Abbvie and Medtronic and consultant fees from Takeda and MSD.

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THE ADDITION OF CASTOR OIL AS A BOOSTER IN COLON CAPSULE REGIMENS SIGNIFICANTLY IMPROVES COMPLETION RATES AND POLYP DETECTION

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Introduction: Incomplete excretion rates are problematic for colon capsule endoscopy (CCE). Widely available booster regimens perform poorly. Recently published same day CCE protocol in IBD using castor oil appeared effective.

Aims & Methods: Our aim was to assess the effectiveness of adding castor oil as an additional booster in our CCE practice.

All patients received split bowel preparation with Moviprep® prior to CCE procedures. Control booster regimen included 750ml of Moviprep® with 750ml of water (booster 1) on reaching the small bowel, a further 250ml of Moviprep® with 250ml of water 3 hours later and a bisacodyl suppository 10mg after 8 hours, if not excreted. Cases followed the same regimen with the addition of 15ml of castor oil given with booster 1. A nested case control design with 2:1 (control: case) ratio was employed. Basic demographics, completion rates, image quality, transit time and polyp detection were compared between groups, using t or chi² tests as appropriate.

Results: In total, 186 CCEs (mean age 60 years (18-97), 56% females, n=104), including 62 cases have been analysed. Cases and controls were matched for age and gender. Overall CCE completion was 77% (144/186) and image quality was adequate/diagnostic in 91% (170/186). The mean transit time was 3.5 hours (0.25-13) and a polyp detection rate was 57% (106/186).

Completion rates were significantly higher with castor oil, 87% cases (54/62) vs 73% controls (90/124), p=0.01. Similarly, polyp detection rates were higher 82% (51/62) vs 44% (55/124), p=0.0001, with an OR of 5.8, 95%CI 2.77-12.21. Transit times were similar, 3.2 and 3.8 hours, respectively. Image quality was similar, reported as adequate/diagnostic in 90% (56/62) vs 92% (114/124).

Conclusion: In our cohort, castor oil addition as a CCE booster significantly improved completion rates and polyp detection in an unselected cohort.

Disclosure: Nothing to disclose

P1392

CLINICAL OUTCOME OF PATIENTS EXAMINED BY SMALL BOWEL CAPSULE ENDOSCOPY WITH NON-SPECIFIC ENTERITIS

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Introduction: As with isolated ileitis on colonoscopy the finding of non-specific enteritis (NSE) on capsule endoscopy (CE) not meeting established diagnostic criteria poses a clinical challenge. There is lack of available evidence to help clinicians to predict significant disease and long-term prognosis. We aimed to define the natural history of NSE in an Irish cohort.

Aims & Methods: A retrospective longitudinal cohort study. Patients with NSE on CE were identified. Clinical records were reviewed, and subsequent investigations, treatments and diagnoses were recorded. Exclusion criteria: known Crohn's disease, enteritis meeting a diagnostic threshold, < 3 months follow up or patients from external institutions. Patients were grouped based on ultimate diagnosis: Crohn's disease (CD), Irritable bowel syndrome (IBS), NSAID enteritis (NSAIDE), no significant disease (NAD), persistent NSE and other non-inflammatory conditions. Clinical and demographic parameters were compared between groups.

Results: 157 (48%) cases were identified, 69 excluded. Of the NSE group (n= 88), 46 (52%) were male, mean age 52, mean follow up 23 months, baseline mean CRP, faecal calprotectin and Lewis Scores were 8.7, 63.8 and 597, respectively. Ultimate diagnoses: NAD 35 (40%), CD 17 (19%), NSAIDs 12 (14%), IBS 14 (16%), persistent NSE 2 (2%), other 8 (9%).

Female gender was associated with IBS (OR 4.7, p < 0.02) and older age with NSAIDs enteritis (mean 64 vs 49 years, p < 0.006). Both NSAIDs and CD were associated with a higher baseline Lewis Score (831.7 vs 308.5, p=0.02). Anaemia was associated with NSAID enteritis (p=0.001). Faecal

calprotectin and CRP were similar among groups. Significantly more CD patients were referred with suspected CD 82% vs 17%, p < 0.009. While anaemia was a more frequent indication in NSAIDE (75% vs 19%, p=0.05).

Conclusion: Our study shows that 33% of patients have clinically significant disease (CSD) on follow up. Clinical suspicion and capsule severity are predictive of CSD.

Disclosure: Nothing to disclose

P1393

A HIGHLY SENSITIVE NEURAL NETWORK-BASED ALGORITHM FOR ASSESSING THE CLEANLINESS OF SMALL BOWEL DURING CAPSULE ENDOSCOPY

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Introduction: Although their use is recommended, the currently available scores for the assessment of cleanliness in small bowel (SB) capsule endoscopy (CE) have poor reproducibility. The aim of this study was to develop and evaluate a neural network (NN)-based algorithm for automated assessment of the SB cleanliness during CE.

Aims & Methods: The proposed NN-based algorithm used a 16-layer Visual Geometry Group architecture. A database of 600 normal third-generation SBCE still frames was artificially augmented to 3000 frames. These frames were categorized as "adequate" or "inadequate" in terms of cleanliness by five expert readers, according to a 10-point scale and served as a reference for the training of the algorithm. A second database comprised 156 different third-generation SBCE recordings, selected from a previous multicenter randomized controlled trial. These recordings were categorized in a consensual manner by three experts, according to a cleanliness assessment scale, and split into two independent 78-video subsets, to serve as a reference for the tuning and evaluation of the algorithm.

Results: A proportion of 79% still frames per video selected as "adequate" by the algorithm was determined to achieve the best performance. Using this threshold, the algorithm yielded a sensitivity of 90.3%, a specificity of 83.3%, and an accuracy of 89.7%. The reproducibility was optimal (kappa=1.0). The mean calculation time per video was 3 ± 1 minutes.

Videos		Algorithm output	Algorithm output	Total
		Adequate	Inadequate	
Experts' consensual evaluation	Adequate	65	7	72
Experts' consensual evaluation	Inadequate	1	5	6
Total		66	12	78

[Performances of the NN-based algorithm outputs for the assessment of SB cleanliness, compared to the consensual overall adequacy assessment.]

Conclusion: Our patent-pending NN-based algorithm allowing automatic assessment of SB cleanliness during CE was highly sensitive and paves the way for automated, standardized SBCE reports.

Disclosure: Xavier Dray, Romain Leenhardt and Aymeric Histace are co-founders and share-holders of Augmented Endoscopy. Xavier Dray has acted as a consultant for Boston Scientific and Norgine, and has given lectures for Fujifilm, Medtronic and Pentax. Romain Leenhardt has given a lecture for Abbvie.

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IMPROVING QUALITY IN COLON CAPSULE ENDOSCOPY; EFFECTS OF DIFFERENT BOWEL PREPARATION REGIMENS

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Introduction: In selected patients, Colon Capsule Endoscopy (CCE) has been recommended by ESGE as an alternative to colonoscopy. The effect of different bowel preparation regimens on Completion Rate (CR) and Bowel Cleansing (BC) is inconclusive.

We aimed to assess the effect of changing from a 4L-PEG (KleanPrep) to a 2L-PEG + ascorbic acid (MoviPrep) bowel preparation on CR and BC.

Aims & Methods: In order to eliminate selection bias, 50 sequential patients who underwent CCE, pre and post change from 4L-PEG to 2L-PEG bowel preparation regimen were included in the study. Both groups used a Phosphosoda (NaP) and Gastrografin booster protocol. Patients' demographics, indications, BC score, CR and findings were recorded. BC was divided into excellent, adequate or inadequate. Completion was defined as passage of CCE beyond the dentate line. Chi squared test was used to compare proportions and p value of < 0.05 was considered significant.

Results: Demographics were similar between the 4L-PEG vs 2L-PEG groups - mean age 50.1 (24-80) vs 44.6 (16-77); 48% (n=24) vs 36% (n=18) males respectively. Chronic diarrhoea was the most common indication for CCE in both groups (28%, n=14 in both). For CR, there was a statistically significant difference favouring 2L-PEG over 4L-PEG; 72% (n=36) vs 54% (n=27), p=0.03. For BC, there were no significant difference between excellent, adequate and inadequate views between the two groups; excellent 22% (n=11) vs 24% (n=12), p=0.8, adequate 66% (n=33) vs 62% (n=31), p=0.7, inadequate 12% (n=6) vs 14% (n=7), p=0.8. Positive findings were similar between groups 50% (n=25) and 56% (n=28), p=0.5.

Conclusion: Reduced volume bowel preparation using a PEG solution which includes ascorbic acid (MoviPrep) improved CCE performance in our patient cohort. Completion rates overall remain suboptimal at 72%. Other potential cofounders in improving CR including changing booster regimen should also be analysed.

Disclosure: Nothing to disclose

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IS IT WORTH REPEATING CAPSULE ENDOSCOPY (CE) IN SUSPECTED SMALL BOWEL BLEEDING?

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Introduction: CE is now the primary investigation for small bowel (SB) bleeding. The utility of repeat CE in patients with ongoing concern of bleeding following initial investigation with CE is unclear. We aimed to review the yield of repeat CE with on-going concern of SB bleeding.

Aims & Methods: Repeat CE procedures over 9 years for a suspicion of ongoing SB bleeding were identified from a database. Patient demographics, CE findings and additional investigations were recorded. Potential factors associated with improved yields were explored.

Results: 339/3,735 (9%) had >1 CE. 152/339 (46%) for bleeding, male 86/152 (57%), mean age 63.9, range 18-92 years, mean CE interval was 461 days (1 - 2576). Haemoglobin (Hb) was available in 81 (52%), low in 65 (80%), mean 11.1.

1stCE findings: normal 19 (13%), angiodysplasia 24 (16%), active bleeding of unclear origin 30 (20%), inflammation 20 (13%), gastric abnormality 20 (13%), incomplete/retained CE 33 (22%), other 6 (4%). 2nd CE completion rate was 96% (n=146) and overall yield was 55% (n=83). Positive or negative index CE did not influence the diagnostic yield of subsequent CE, 8/19 (42%) normal vs 75/133 (56%) abnormal, p=0.1. Patients with active bleeding or angiodysplasia were almost 3 times more likely to have a positive 2nd CE (OR = 2.8, p = 0.004, 95%CI 1.3 to 5.6). Older patients (>70) were also more likely to have a positive 2nd CE, OR 2.3, p=0.01, 95%CI 1.17 to 4.45. Subjects with index retained/incomplete CE were more likely to have a subsequent incomplete study, OR 7, p = 0.01, 95%CI 1.55 to 30.62.

Conclusion: Second look CE in obscure bleeding can be an effective clinical tool with a diagnostic yield of 55%. Along with clinical suspicion, older age and initial small bowel bleeding/vascular lesion are predictive of higher yield.

Disclosure: Nothing to disclose

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COMPARISON OF STANDARD CAPSULE ENDOSCOPY VERSUS MAGNETICALLY CONTROLLED CAPSULE ENDOSCOPY (MACE) TO EVALUATE GASTRIC DISORDERS IN PATIENTS REFERRED FOR SMALL BOWEL CAPSULE INVESTIGATION

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Introduction: While capsule endoscopy is traditionally the gold standard diagnostic method of the small bowel disorders, the novel magnetically controlled capsule endoscopy (MACE) system has been developed to investigate both stomach and small bowel mucosal surface without patient sedation and discomfort.

Aims & Methods: In the present study our aim was to compare standard Intramedic SB capsule endoscopy (SBCE) and the Ankon MACE system in the evaluation of esophageal and gastric disorders in patients referred for small bowel capsule endoscopy with similar indications.

504 consecutive outpatients referred for small bowel capsule endoscopy were enrolled, prospectively. Preparation for capsule endoscopy was liquid diet + 1L PEG on the previous day and simethicone, pronase B with 700-1000 ml clear water just before the examination. Esophagus was examined on left lateral position with 45° elevated head, and then the stomach was examined in the supine, left and right lateral decubitus position. Finally, all patients underwent a complete small bowel CE study protocol, too. In 30 patients the stomach was investigated with the Intramedic 1600 SBCE, relying only to the spontaneous peristalsis and in 474 patients the gastric mucosa was explored with the Ankon MACE system with active magnetic control of the capsule endoscope in the stomach, applying three different standardized pre-programmed computerized algorithms.

Results: When we compared the mean gastric and small bowel transit time with MACE versus SBCE system, no significant differences were demonstrated, as follows: 50,2 min and 200,2 min versus 46,1 min and 226,2 min, respectively. When three independent endoscopist scored the percentage of the visibility of the entire gastric mucosa, MACE appeared to have a significantly better visualization scores as compared to SBCE: 95% vs 65%. Moreover, the overall diagnostic yield to detect any gastric mucosal abnormality or focal lesion were higher with MACE as compared to SBCE (overall diagnostic yield to detect any abnormality: 81,3% vs. 75,9%, erosive reflux: 27% vs. 24%, proximal gastritis: 32% vs 34%, antral gastritis: 32% vs 27%, foveolar hyperplasia: 13% vs 3%, gastric polyp: 3,4% vs. 1,1%, erosion or ulcer: 2,5% vs 0% and cancer: 0,4% vs 0%). Manually controlled, active magnetic movement of the Ankon capsule across the pylorus was successful with MACE in 59,1% of all patients. UBT test revealed H. pylori positivity in overall 25% of all patients.

Conclusion: MACE is an effective and safe diagnostic method to evaluate upper GI mucosal lesions in patients referred for small bowel capsule study. As compare to SBCE, application of MACE can significantly increase the visualization and the diagnostic yield of gastric mucosal abnormalities without any reduction the diagnostic accuracy of the capsule endoscopy in the small bowel. Therefore, MACE with the new Ankon capsule endoscopy system is a useful diagnostic method to evaluate gastric and small bowel mucosa and can be the future non-invasive screening tool to decrease morbidity and mortality of benign and malignant upper GI disorders.

Disclosure: Nothing to disclose

P1397

THE ROLE OF UPPER GASTROINTESTINAL ENDOSCOPY IN EVALUATING FINDINGS ON CROSS-SECTIONAL IMAGING

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Introduction: Cross sectional imaging (CTAP) is frequently undertaken in patients referred with suspected malignancy, but can often reveal unexpected incidental findings ("Incidentalomas"). A recent meta-analysis highlighted that incidentalomas are found in 38% of patients undergoing CT colonoscopy (1). This study determines if specific features on CTAP need evaluation with OGD.

Aims & Methods: This was an observational cohort study of patients undergoing OGD at a university teaching hospital from Oct 2008-18 primarily due to abnormalities on CTAP.

Endoscopy data (endosoftR) were cross-referenced with radiology reports, histology and electronic hospital records. Radiological data were categorized according to anatomical location, type of abnormality (mass, thickening, dilatation, lymphadenopathy) and the likelihood of malignancy (based on clinical presentation) dichotomised as possible/probable or unlikely/incidental.

Results: 256 patients (148 males), Mean age = 64.7 (st dev = 14.1) were included of which 17 cancers were found during endoscopy (Oesophagus n=2, stomach n=12, Duodenum n=3).

In those patients in whom cancer was not suspected (n=144), but with the CTAP appearances of a mass (n=14) 6/14 were found to have cancer at OGD compared to 0/27 in whom cancer was suspected (chi-square =10, p=< 0.5).

In contrast, the CTAP findings of dilatation/distension or other non-specific reported abnormalities (n=63) were not associated with cancer regardless of whether cancer was suspected or not.

Of patients in whom thickening/oedema/fat stranding was reported, cancer was found in 1/78 as incidental findings compared to 7/48 where cancer was suspected (Chi-square= 9, P=< 0.5).

In those patients whom cancer was suspected, the finding of a mass was not associated with the endoscopic findings of malignancy (0/27). Two patients with lymphadenopathy (2/13) were found to have cancer with thickening/oedema/fat stranding representing 7/48.

The CTAP findings of dilatation/distension or other non-specific reported abnormalities n=63 were never associated with cancer in either group.

Conclusion: Our results, from the largest study to date, suggest that the CT findings of dilatation/distension or other non-specific abnormalities are likely to be incidental findings and do not require further endoscopic evaluation.

However the CTAP appearances of a mass regardless of the clinical context warrant assessment by OGD. In the context of suspected cancer, thickening/oedema/fat stranding also warrants OGD.

References: O'Sullivan Jack W, Muntinga Tim, Grigg Sam, Ioannidis John P A. Prevalence and outcomes of incidental imaging findings: umbrella review BMJ2018; 361:k2387

Disclosure: Nothing to disclose

P1398

EUS-GUIDED INTRAHEPATIC ACCESS FOR BILIARY DRAINAGE: A RETROSPECTIVE TERTIARY CENTRE EXPERIENCE WITH SUBGROUP MATCHED COMPARISON TO PERCUTANEOUS DRAINAGE

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Introduction: EUS-guided intrahepatic access for biliary drainage (EUS-IBD) still lacks convincing evidence on advantages and risks over comparators, such as percutaneous biliary drainage (PTBD), as well as on comparisons between the different EUS-IBD approaches (i.e. rendez-vous (RV), antegrade stenting (AS) and hepatico-gastrostomy (HG)).

Aims & Methods: We retrospectively revised the 8-year experience of a tertiary, academic, referral centre.

All consecutive EUS-IBDs performed between 2012-2019 were included. RV, AS and HG were separately analysed. Patients with hilar/intrahepatic

stenosis or surgically-altered anatomy undergoing EUS-IBD were matched 1:1 with patients undergoing PTBD. Efficacy, safety and events during follow-up were compared.

Results: 104 EUS-IBDs were identified (malignancies=83.7%; post-surgical anatomy=22.1%). Distal, hilar and anastomotic strictures represented 50%, 28.9% and 14.4% of indications.

Overall technical success was 89.4%, while clinical success (>25% decrease in bilirubin levels or successful management of choledocholithiasis) was 96.2%. Using the ASGE lexicon, overall, severe and fatal complications occurred in 23.3%, 2.9% and 0.9% respectively. Median hospital stay was 7[3-10] days, 4.5[1-9] in case of no complications.

The 16 RV, 43 AS and 45 HG were similar with regards to efficacy and safety, with comparable dysfunction rate during follow-up. Benign indications were more common among RV, whilst hilar stenoses, surgically-altered anatomy and disconnected left ducts were identified more frequently in the HG group. HG performed with partially-covered specifically-designed self-expandable metal stents (SEMS) showed shorter procedural length (25 vs. 48 minutes, $p=0.004$) and a trend towards lower stent dysfunction (6.7% vs. 30%, $p=0.09$) compared to previous approaches (e.g. covered SEMS or overlapping uncovered/covered SEMS).

Among patients with proximal stenosis/surgically-altered anatomy, EUS-IBD vs. PTBD showed higher clinical success (97.4% vs. 79.5%, $p=0.01$), reduced post-procedural pain (17.8% vs. 44.4%, $p=0.0044$), median hospital stay (7.5 vs 11.5 days, $p=0.007$), stent dysfunction rates (15.8% vs. 42.9%, $p=0.01$) and mean number of re-interventions (0.4 vs. 2.8, $p<0.0001$). Technical success and procedure duration were similar.

Conclusion: The intrahepatic route for EUS-guided biliary drainage has high technical and clinical success with an acceptable safety profile. Compared to RV and AS, HG showed similar outcomes, which are likely to improve with the use of dedicated tools. For hilar/intrahepatic strictures and surgically-altered anatomy specifically, EUS-IBD showed superiority to PTBD on various levels. Based on these data and on previously published literature, we believe that the time has come to include EUS-IBD in the armamentarium of technical procedures available in managing complex biliopancreatic diseases. Future comparative data will further clarify the most optimal patient-procedure match.

Disclosure: Schalk van der Merwe holds the Cook chair in Interventional endoscopy and holds consultancy agreements with Cook, Pentax and Olympus. Wim Laleman co-chairs the Boston-Scientific Chair in Therapeutic Biliopancreatic Endoscopy with Schalk Van der Merwe and has consultancy agreements with Boston Scientific and Cook. Hannah van Malenstein holds a consultancy agreement with Boston-Scientific

P1399

MECHANICAL PROPERTIES AND DEGRADATION PROCESS OF SELF-EXPANDABLE BIODEGRADABLE STENTS

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Introduction: Because of the different degradation time depending on the raw materials making the biodegradable stents (BS), clinical outcomes are different.

Aims & Methods: The aim of this study was to evaluate the mechanical properties and degradation process of different prototypes of BS for a given period of time.

Using an in vitro bile flow phantom model, we compared the degradation time, radial force changes, and morphologic changes among four different proto-types of BS: polydioxanone (PDO) BS, polyglycolide (PGA) BS, polydioxanone-poly(lactic acid) (PDO-PLLA) sheath core BS, polydioxanone-magnesium (PDO-Mg) sheath core BS. Using an in vivo swine bile duct dilation model, we performed a direct peroral cholangioscopy (DPOC) examination for observing biodegradation process and related complications every two weeks.

Results: Four different BS were retrieved and analyzed every two weeks in the bile flow phantom model. The PGA BS and PDO-Mg BS showed rapid radial force reduction and morphological changes occurred and totally degraded within six weeks. The PDO BS and PDO-PLLA BS degraded after maintaining high radial force and original shape for more than 12 weeks. Twenty-four PS were inserted into the dilated bile ducts of 12 swine models. In animal model, DPOC examination revealed that PDO BS and PDO-PLLA BS were well maintained the original shape until 12 weeks, but PDO BS turned into more fragmentations and were accompanied by a lot of stones.

Conclusion: Our results showed that PDO-PLLA BS maintained their original shape and radial force for a relatively long time and minimized complications.

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P1400 WITHDRAWN

P1401

PREMIUM NON NOCERE: ENDOSCOPIC BILIARY STENTS FOR CHOLANGITIS COMPLICATING CHOLEDOCHOLITHIASIS IN THE ELDERLY ARE SAFE AND CAN BE LEFT FOR UP TO 25 MONTHS

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Introduction: Treatment of cholangitis complicating choledocholithiasis includes biliary sphincterotomy and stone extraction. In certain cases of elderly comorbid patients with high risk for definitive endoscopic treatment, biliary stenting is the main measure for relieving biliary obstruction.

Aims & Methods: We aimed to report the safety of retained biliary stone in elderly patients with cholangitis complicating choledocholithiasis. A multi-center, retrospective case-control study conducted at two Israeli medical centers from January 2013 to December 2018 including all patients 18 years of age or older who underwent ERCP and biliary stent insertion for the treatment of acute cholangitis due to choledocholithiasis.

Results: Three-hundred and eight patients were identified. Eighty-three patients had retained long-term biliary stents of more than 6 months (group A) from the insertion compared to 225 patients who their biliary stents removed within 6 months period (group B). The average ages of group A and B were 83.5 ± 4.8 years and 61.3 ± 17.9 years respectively ($P < 0.001$). Sixty-five percent and 63% of the patients were males in groups A and B respectively. The mean follow-up in group A was 66.1 ± 16.3 vs. 11.1 ± 2.7 weeks in group B. Overall complications during the follow-up were similar between group A and B (6% vs. 4.9%, OR 1.24, Chi square 0.69). similarly, the rate of each complication alone was not different comparing group A to group B (3.6%, 1.2% and 1.2% vs. 2.7%, 0.44% and 1.8%) for cholangitis, stent related pancreatitis and biliary colic, respectively (Chi square 0.85). Even after 12 months, the rate of overall complications and each complication alone were not higher compared to less than 12 months (Chi square 0.72 and 0.8, respectively).

Conclusion: Endoscopic biliary stenting for cholangitis complicating choledocholithiasis is safe for the long-term period without increase in stent related complication.

Disclosure: Nothing to disclose

P1402

TEMPORARY PLACEMENT OFF A FULLY-COVERED METALLIC STENT FOR DOMINANT STRICTURE AMONG PRIMARY SCLEROSING CHOLANGITIS (PSC) PATIENTS: SAFETY AN EFFICACY

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Introduction: When dominant stricture (DS) is diagnosed either prior to ERCP or during ERCP, there are multiple therapeutic options available to the endoscopist including dilation and stenting, each with their own benefits and drawbacks.

The aim of the current study is to assess the safety and efficacy of fully-covered self-expandable metal stent (FCSEMS) in management of DS among PSC patients.

Aims & Methods: We include PSC patients with refractory DS, defined as strictures resistance to conventional therapy (balloon dilatation, or and plastic biliary stent insertion) longer than three months. FCSEMS was placed for 3 months.

The primary outcome was the DS resolution at stent removal. And the secondary outcome was the DS recurrence as well as development of cholangitis, jaundice, and elevation of liver functions test and or refractory pruritus.

Results: 15 patient were enrolled between January 2016 to May 2018, FCSEMS was placed in all the 15 patients with DS, one patients need premature removal of the FCSEMS due to cholangitis on day 46 from the stent placement. Overall 14 patients complete planned 3 months, and after 90 days all the stents were softly removed.

The rate of DS resolution was, 43.7%. And recurrence occurred in 17.8 during median follow-up of 12 months. Improvement on liver function test, pruritus and weakness were observed in 28.5%, 57%, and 64.2% respectively. In all 14 patients MAYO score was improved by median 26%. Adverse event was observed in 28.5% during 12 months follow-up, 1 case of cholangitis, 2 cases of biliary pancreatitis, 1 stent partially migrated to duodenum.

Conclusion: Temporary FCSEMS was feasible, safe and effective treatment option among refractory DS PSC patients.

Disclosure: Nothing to disclose

P1403

EFFECTIVENESS AND SAFETY OF COVERED SELF-EXPANDING METAL STENT IN BENIGN BILIARY STENOSIS DUE TO CHRONIC PANCREATITIS: OBSERVATIONAL RETROSPECTIVE STUDY

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Introduction: The most frequent causes of benign biliary stenosis are stenosis due to surgery and fibrosis secondary to chronic pancreatitis (CP). The temporary placement by ERCP of multiple plastic prostheses in parallel has been the endoscopic treatment of choice, although in recent years

various studies have shown favorable results through the use of fully covered metal prostheses (cSEMS), with high clinical success rates and fewer endoscopic procedures.

Aims: To analyze the technical, clinical success and the complications associated with the placement of cSEMS in benign biliary stenosis secondary to CP in our center.

Methods: Retrospective study between January 2012 - December 2018. Epidemiological and analytical variables were analyzed, also data from endoscopic procedure (stent residence time, technical complications, related incidents) and clinical (percentage of recurrences/surgical indications).

Technical success was defined as the correct placement and withdrawal of the cSEMS during the ERCP and clinical success as an analytical improvement (normalization of bilirubin) at 6 months post-withdrawal of the cSEMS. Stent residence time (patent) was defined as the time in days from stent placement to withdrawal (scheduled, by occlusion / migration or by surgical intervention).

Results: 37 cSEMS were included in 20 patients (85% men; mean age 52.55). The mean basal bilirubin was 5.34mg/dL. In 75% of the patients, cytology and/or stenosis biopsy was performed during ERCP, with no evidence of malignancy. However, in 2 cases the stenosis later turned out to be of malignant etiology.

Technical success was 100% in stent's placement and removal. There were 25 complications (67.27%), with obstruction and proximal migration being the most frequent complications.

The average residence time of the stent was 305 days. The average bilirubin at 6 months post-stent withdrawal was 1.17mg/dL, achieving clinical success in 70% of cases. 10% required surgical intervention due to recurrence of stenosis.

Conclusion: The placement of cSEMS for the treatment of benign biliary stenosis due to chronic pancreatitis is an effective and safe method that can be considered as an alternative to the placement of multiple plastic prostheses.

Our series consists of patients of habitual clinical practice, in which we have observed a clinical success rate of 70%, similar to previous data reported in multicentre trials with clinical success rates between 47-66% in post-withdrawal periods between 3-12 months.

Disclosure: Nothing to disclose

P1404

INTRAOPERATIVE CHOLANGIOSCOPY WITH THE SPYGLASS DS SYSTEM IN PATIENTS WITH OR WITHOUT SURGICAL ALTERED BILIARY ANATOMY: TECHNICAL FEASIBILITY AND CLINICAL RELEVANCE

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Introduction: Digital single-operator cholangioscopy (dSOC) has revolutionized bile duct visualization by enabling endoscopic characterization of malignant on non-malignant changes as well as performing therapeutic interventions during endoscopic retrograde cholangiography (ERC). Here we demonstrate the intraoperative approach with access to the biliary system with the dSOC-device during open liver surgery. We further analyze the impact of direct intraoperative dSOC (IC) on the clinical and surgical management.

Aims & Methods: 10 patients (6 male and 4 female, 5 pediatric patients, average age of 24.7 years, range 0.5-66 years) were included in this series. 6 Patients had liver transplantation (LTx) before, 3 with biliodigestive anastomosis (BDA) and 3 with E/E-cholecho-choledochostomy. One pediatric patient had a BDA without LTx due to inflammation and secondary sclerosing cholangitis after premature birth and septic complications and another patient biliary reconstruction with the appendix after small-bowel ischemia. Retrospectively, we analyzed the biliary access route of the dSOC device, intraoperative findings, therapy and if IC had impact of the surgical and/or clinical management.

Results: In case of BDA, biliary access was achieved by incision of the intestinal loop of the Roux-en-Y bypass and passing the anastomosis into the biliary system in 3 patients. In one patient with BDA the biliary system was entered after hepatic left resection. In patients with unaltered anatomy, the biliary system was entered by the cystic duct (2 patients), from peripheral opened liver segment II (1 patient), by choledochotomy (2 patients) and by duodeno-appendico-hepaticostomy (1 patient).

All IC procedures were neither therapeutic with concrement extraction, biliary dilation, electrohydraulic lithotripsy (EHL; 3 patients) or with direct impact on the surgical management by:

- Determining the resection margins in ITBL lesions or bile duct necrosis,
- Decision for performing a BDA,
- Extend surgery after visualization of distal cholangiocarcinoma and
- Decision against further surgical resection but scheduling for liver transplantation.

Conclusion: dSOC has been demonstrated to be an effective diagnostic and therapeutic tool during standard ERC. IC with the SpyGlass DS device is technical feasible with various possibilities to access the biliary system. In our case series, the clinical impact was high and guided or even changed the surgical and clinical management in all patients. This is of great importance as half of the patients were pediatric patients, also with previous LTx.

Disclosure: Nothing to disclose

P1405 WITHDRAWN

P1406

COMPARING 10 FRENCH STRAIGHT AND 7 FRENCH DOUBLE PIGTAIL STENTS FOR PATIENTS WITH INCOMPLETE COMMON BILE DUCT STONE CLEARANCE ON INDEX ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Introduction: Biliary stenting is often needed for patients with incomplete common bile duct (CBD) stone clearance during index endoscopic retrograde cholangiopancreatography (ERCP). Ten French (Fr) straight and 7Fr double pigtail plastic stents are 2 commonly used stents in this scenario. It is not known which of the 2 stents are associated with less complications and better outcomes.

Aims & Methods: We aim to compare differences between the 2 stents in the index and follow-up ERCP. Primary outcome was stent complication rates. Secondary outcomes were change in stone number, change in stone

size and difference in the number of ERCP to clear all the CBD stones. A retrospective cohort study was done in a single general hospital in Singapore. All patients who had ERCP for CBD stones and had incomplete stone clearance during the index ERCP with a single plastic stent inserted (10Fr straight or 7Fr double pigtail) were included. Patients with other stent types, more than 1 stent inserted or defaulted follow-up ERCP were excluded. Patients were then divided into 2 groups: those with 10Fr stent and those with 7Fr stent.

Results: During 2016 and 2017, a total of 686 ERCP were carried out. Of these procedures, 527 (76.8%) were for CBD stones. One hundred and six (20.1%) had either a 10Fr or 7Fr stent placed for incomplete stone clearance. 75 (70.8%) had 10Fr stent placed and 31 (29.2%) had 7Fr stent placed. The 10Fr group had significantly higher proportion of patients with higher American Society of Anesthesiologist (ASA) scores. The 7Fr group had significantly larger proportion of patients with large CBD stones (Table 1). There were 12 complications in the 10Fr group (16%) and 9 in the 7Fr group (29%) although this was not statistically significant ($p=0.18$).

The majority of the complications (76.1%) were stent migrations and there were equal number in each group. Other complications included: 3 blocked stents in the 10Fr group and 1 in the 7Fr group as well as 1 cholangitis and pancreatitis in the 10Fr group.

Change in number of CBD stones in the index and follow-up ERCP was similar in both groups. Not surprisingly, there were significantly more patients with large stones in the 7Fr group during follow-up ERCP and this group also had significantly greater number of patients requiring >2 ERCP to clear the CBD.

		7Fr (n=31)	10Fr (n=75)	p value
Age (mean)	Years	72.9	65.3	0.15
Sex	Female	15	23	0.12
	Male	16	52	
ASA	1	8	6	*0.03
	2	18	40	
	3	4	26	
	4	1	3	
Presentation	Cholangitis	18	52	0.54
	Biliary colic	2	4	
	Pancreatitis	2	2	
	Incidental stone on scan	9	17	
Number of stones	Single	13	29	0.825
	Multiple	17	45	
Size of stones	Small	14	52	*0.04
	Large	15	22	

[Table 1: Baseline characteristics]

Conclusion: Our study demonstrated that use of a 7Fr double pigtail stent may be associated with higher complication rates. The majority of complications are stent migrations. Both stents are likely to be equally efficient in reducing CBD stone burden. These need to be confirmed with a prospective study.

Disclosure: Nothing to disclose

P1407 WITHDRAWN

P1408

COMPARISON OF ENDOSCOPIC RETROGRADE STENT PLACEMENT VIA TRANS-PAPILLAR VERSUS SUPRA-PAPILLAR METHOD FOR MALIGNANT BILIARY OBSTRUCTION

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Introduction: The main causes of the stent failure in malignant biliary obstruction were food reflux and migration, had reported 15.4 % and 7.7 %, respectively. Recently, various types of anti-reflux metal stents have been developed, but there was no consistent evidence to show superiority compared to uncovered metal stents.

Aims & Methods: We evaluated the differences in treatment outcome of metal stent insertion across the major papilla (trans-papillar method) versus above the major papilla (supra-papillar method) among Korean patients with malignant obstruction on the common bile duct. This will help to elongate the patency of the stent for palliative treatment in malignant biliary obstruction of the common bile duct. **Methods:** A total of 100 patients with malignant biliary obstruction at the extrahepatic duct who underwent endoscopic retrograde biliary drainage in Asan Medical Center were included in this study. Patients with malignant biliary obstruction, including the hepatic hilar stricture, were excluded from this study. 43 patients and 57 patients were treated with stent insertion via supra- and trans-papillar method, respectively. Stent patency and causes of stent failure were assessed.

Results: The mean stent patency times were 183.5 days $\pm$ 146.0 and 132.0 days $\pm$ 146 in supra- and trans-papillar method, respectively. Cumulative stent patency was significantly higher in supra-papillar method than in trans-papillar method ($P = 0.04$). Stent failure appeared in 13 and 24 patients, respectively (30.2 %, 42.1 %, $P = 0.007$). Logistic regression analysis shows that the only significant associated factor of stent failure was stent insertion via trans-papillar method (OR 3.24, CI 1.03 - 10.13, $P = 0.049$). The four major causes of stent failure in trans-papillar method were distal migration, food reflux, tumor growth in stent and sludge, 54.2 %, 16.7 %, 16.7 %, 8.3%, respectively. In contrast, in supra-papillar method, those were tumor growth in stent, tumor growth over stent, food reflux and sludge, 69.2 %, 15.4%, 7.7%, 7.7 %, respectively.

Conclusion: Endoscopic retrograde stent placement via supra-papillar method may achieve longer stent patency and a lower stent failure rate compared with trans-papillar method. For patients with malignant biliary obstruction on the common bile duct, supra-papillar method should be considered.

Disclosure: Nothing to disclose

P1409

LUMEN-APPOSING METAL STENT THROUGH THE MESHES OF THE DUODENAL SELF-EXPANDABLE METAL STENT: IS IT REALLY FEASIBLE?

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) represents the gold standard for malignant jaundice palliation but it can be challenging when a duodenal self-expandable metal stent (SEMS) is indwelled.

Aims & Methods: The aim of our study is to retrospectively evaluate the technical feasibility, clinical outcome and technical and clinical adverse events (AEs) related to LAMS placement through the duodenal meshes (TTM).

Results: Data from 23 patients (11 F and 12 M; mean age: 69.5 ± 11 years old) were collected. In 17 patients (73.9%) TTM LAMS placement was performed as first intention and in 6 patients (26.1%) was performed after a failed ERCP attempt of cannulation of the common bile duct (CBD). Pre-cut was not performed in any of the cases. 13 patients had an advanced pancreatic head neoplasia (56.5%) unfit for surgery and 10 patients (43.5%) others (advanced ampulloma; breast cancer metastases; distal CBD neoplasia; neuroendocrine tumour; duodenal adenocarcinoma; gallbladder neoplasia; malignant recurrence of a previous distal esophageal adenocarcinoma). One adverse event (AEs) was experienced, an early migration of the LAMS out of the common bile duct (CBD) into the duodenal lumen, immediately after its deployment (4.3%) in a patients underwent chemo-radiotherapy (CT-RT).

Conclusion: Concomitant malignant duodenal and biliary obstruction are rare and challenging conditions. In these particular cases the placement of duodenal SEMS is mandatory before to proceed to ERCP. If ERCP fails EUS biliary drainage by LAMS is indicated. If the only target-point to drain CBD or gallbladder is through the duodenal meshes, the procedure is technical feasible, paying attention to previously treated patient by RT. A larger prospective series are needed to confirm our initially data.

Disclosure: Nothing to disclose

P1410

ENDOSCOPIC SMALL BOWEL DILATIONS IN PATIENTS WITH CROHN'S DISEASE: A DANISH NATIONWIDE COHORT STUDY, 1997-2015

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Introduction: Small bowel strictures in patients with Crohn's Disease (CD) are a common complication, which might occur as part of progressive inflammation or following surgical bowel resections. Endoscopic dilation is an emerging therapeutic approach which is minimal invasive and preserving bowel length. Despite the apparent potential, only few selected patients receive this treatment.

Furthermore, the reported effectiveness varies and might be hampered by referral bias, and data from population-based cohorts are lacking. The aim of this study was to assess the use of endoscopic dilation procedures in adult CD patients with small bowel strictures in a 19-year period.

Aims & Methods: This nationwide cohort comprised all individuals aged 18 years or older who were diagnosed with CD in Denmark between January 1st, 1997 and December 31st, 2015, according to the National Patient Registry (NPR). Data on endoscopic and surgical procedures as well as on relevant medications were retrieved from the NPR and The Danish National Health Service Prescription Database. We defined the need for surgery as a failure of the dilatation procedure.

Results: The cohort consisted of 9,737 incident CD patients, that were followed for a median (IQR) 8.2 (4.1-13.3) of years. During the observation period, a total of 90/9,737 (1%) patients in the cohort had an endoscopic small bowel dilation performed.

The subgroup with 49/90 (54%) patients having de novo stricture was dilated a median of 5.5 (0.5-9.9) years after the CD diagnosis. A median of 1 (1-1) dilation was performed in these patients. After a follow-up period of median 3.4 (1.8-5.0) years, de novo strictures treated only with one dilation and no subsequent small bowel surgery accounted for 29/49 (59%) of the cases. A total of 7/49 (14%) patients had more than one endoscopic dilation (median of 3 dilations in total) but no small bowel surgery.

After a median of 7.2 (2.4-13.2) months after their first dilation, 13/49 (27%) underwent small bowel surgery. At the time of the first dilation in the de novo stricture subgroup, 18/49 (37%) and 7/49 (14%) were treated with immunomodulators and biologics, respectively. The other dilated subgroup was 41/90 (46%) patients with post-surgical strictures. They were dilated after a median of 6.5 (2.5-10.2) years following small bowel surgery. A median of 1 (1-2) dilation was performed in these patients. After a follow-up period of median 5.4 (1.8-7.6) years, post-surgical strictures treated only with one dilation and no further small bowel surgery accounted for 20/41 (49%) of the cases. Redilation with no further small bowel surgery occurred in 11/41 (27%) (median of 2 dilations in total). After a median period of 8.4 (3.6-14.4) months after their first dilation, 10/41 (24%) patients subsequently underwent small bowel surgery. At the time of dilation in the post-surgical stricture subgroup, 15/41 (37%) and 6/41 (15%) were treated with immunomodulators and biologics, respectively. In a multivariate cox-regression model, immunosuppressive and/or biologic treatment in the 6-month period after first endoscopic dilation did not reduce the risk of subsequent small bowel surgery (HR: 1.53 (0.64-3.70), p=0.34).

Conclusion: In this nationwide study, only few patients underwent endoscopic small bowel balloon dilation. However, during a median follow-up of 5 years following endoscopic dilation, the majority of patients remained

without the need for surgery. This suggests that endoscopic small bowel dilation is an effective treatment option, which may be offered to more patients.

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P1411

ENDOSCOPIC STRICTUROTOMY FOR REFRACTORY ANASTOMOTIC STRICTURES AFTER ESOPHAGECTOMY: A PILOT STUDY

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Introduction: Refractory esophageal anastomotic strictures are the frequent challenge for the endoscopists. The current therapeutic strategies require more repeated sessions of endoscopic therapies but still not maintain long-term patency.

Aims & Methods: We propose a modified incision and cutting method named as Endoscopic Strictureotomy (ES) to treat refractory esophageal anastomotic strictures. The efficacy of the novel method is described. From September to December 2019, four patients diagnosed as refractory esophageal anastomotic strictures who had undergone more than 3 sessions (3-11 sessions) of EBD (up to 15 mm in diameter) were treated with ES.

The steps of ES: one single incision is begun at the anastomotic orifice, and then cutting extended upward in the cephalic direction.

The aim of incision is to destroy enough volume of fibrotic tissues with less damaged mucosae. The required length and depth of incision is according to the actual length and thickness of fibrotic tissues. The primary endpoint was the duration of dysphagia relief. The sessions and intervals between endoscopic therapies within 6 months follow-up were counted. The complications of treatment were also recorded during the following up.

Results: Dysphagia was relieved in all four patients after ES procedures. The duration of dysphagia relief after ES were 24 weeks (range 20 to 32 weeks) during the follow-up of 6 to 8 months. There were 2 patients with persistent reflux esophagitis requested the second ES because of mild dysphagia (grade II) after 8 weeks and the symptoms were completely relieved.

There was no failure or complication during following up.

Conclusion: Endoscopic strictureotomy seems to be a good treatment modality for refractory esophageal anastomotic strictures.

However, prospective clinical trial with large scale are needed to confirm its utility and place in the management of refractory anastomotic strictures.

Disclosure: Nothing to disclose

NO.	1	2	3	4
Sex (M/F)	M	M	M	M
Age (years)	42	46	66	71
Leakage (N/Y)	N	Y	Y	N
Anastomosis Location#(cm)	34	39	30	22
Dysphagia Grade&	IV	IV	IV	IV
Total Sessions	6 EBD + 3 EI	2 EBD+ 2 Stenting	5 EBD + 3 EI	1 EBD +2EI
Intervals between sessions (wk)	5.3(4-8)	3(3-3)	5.3(4-8)	7 (5-9)
Diameter of anastomosis(cm)	0.2	0.2	0.3	0.5
Length of stricture (cm)	0.5	0.5	0.5	0.5
After ES				
Dysphagia Grade				
0 week	I	I	I	I
4 week	I	I	I	I
8 week	II	II	I	I
12 week	I	I	I	I
24 week	I	I	I	I
Diameter of anastomosis (cm)	1.0	1.0	1.0	1.0
Length of incision(cm)	1.0	1.0	1.0	1.0
Complications	None	None	None	None
Hospital stays (days)	1	2	1	2
Procedure Time (min.)	21	20	19	21
Sessions of ES	2	2	1	1

[Table. The basic characteristics of patients with anastomotic stricture and the results of ES]

Note: *Anastomotic location means the centimeters of distance from incisor teeth to anastomotic orifice. *Dysphagia grade I, normal passage of solids and liquids; grade II, dysphagia for solids; grade III, dysphagia for semisolids; or grade IV, dysphagia for liquids *EBD, endoscopic bougie dilation; EI, endoscopic electro-incision; * the two patients with persistent reflux esophagitis underwent second ES because of mild dysphagia after 8 weeks.

P1412

ESOPHAGEAL DILATATIONS - TOO MANY CHEFS SPOIL THE BROTH

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Introduction: In British endoscopy units, dilatations are done by most endoscopists. We were surprised to learn from our admin staff, that patients often expressed strong preferences to have their dilatations done by particular endoscopists. Therefore we set out to explore if there was a difference in the performance and outcomes between endoscopists.

Aims & Methods: We looked at dilatations done for oesophageal strictureing 2017-2019 in a large tertiary UK referral centre. Patients having had Nissen's procedures and neoplastic strictures were excluded. In our analysis of Quality, we excluded endoscopists who had carried out fewer than 20 procedures. Success, Relapse, Primary Failure (refractory stricture), Secondary Failure (recurrent stricture), Programme Failure (lost or delayed appointments) and Patient defaulting from programme were defined. The requirement of a stent was regarded as a primary failure of the dilatation programme.

Results: 1177 dilatations were carried out in 204 patients. 947 of these were carried out by 14 Consultants. The strictures were of the usual aetiologies seen in most endoscopy units and included; peptic strictures (106 pts), EMR (7 pts), RFA (7 pts), radiotherapy (19 pts), anastomotic (34 pts), eosinophilic (8 pts), Schatzki rings (7 pts), and 16 other aetiologies strictures such as Crohn's, lichen planus, caustic, bisphosphonates and webs. Most patients (144) required 3 or fewer dilatations. The mean number of dilatations was 3.7 (IQR 1.4 - 6.0, mode 1, median 2).

Half of the 106 patients with peptic strictures were successfully managed by our dilatation service, although 24 strictures recurred after 6 months. As recognised in previous studies, radiotherapy and anastomotic strictures were most difficult to manage requiring an average of 5 dilatations and ultimately half requiring a stent. Similarly, patients with longer peptic strictures, required significantly more dilatations than patients with strictures shorter than 3cm (4.9 dilatations vs 10.4 dilatations, $p < 0.0029$). There were 2 perforations and 3 admissions with post procedural bleeding.

We were surprised to find that when 4 particular endoscopists were involved, strictures were significantly more likely to be successfully dealt with (68% success rate vs 52% success rate, $\chi^2 p < 0.000012$). The reasons for this appeared to be three-fold. Firstly, their first dilatation was significantly wider (15.2mm vs 13mm, Student t-test $p < 0.00001$).

Secondly, they organised the next dilatation sooner (average of 25 days later vs 30 days, $p = 0.01$) and finally, at each dilatation their average step-up in dilatation was significantly greater than their colleagues (1.3mm vs 1mm, $p < 0.001$).

Conclusion: This is the first study of oesophageal dilatations to highlight that it is not just the aetiology of the stricture which predicts outcomes. Even more important is the endoscopist. Endoscopists who dilate further and organise a follow up dilatation sooner have significantly better outcomes. In the UK, we no longer schedule larger polypectomy on 'any endoscopy list'. Similarly, our data suggests that oesophageal dilatations should only be scheduled on dedicated lists staffed by endoscopists with the necessary skills and confidence to deal with oesophageal strictures.

Disclosure: Nothing to disclose

P1413

ENDOSCOPIC TREATMENT OF FUNCTIONAL AND ORGANIC STENOSIS AFTER SLEEVE GASTRECTOMY: EFFICACY OF DILATION AND LONG-TERM FOLLOW-UP

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Introduction: Sleeve gastrectomy (SG) is complicated in about 5% of cases by leakage or stenosis. Post-SG stenoses are either organic, due to fibrotic narrowing of gastric lumen, and/or functional, due to the presence of a twist or a kink of the residual stomach. Both hydrostatic (HD) and pneumatic dilation (PD) have been used in case series for post-SG stenosis treatment, but data remain scarce. We describe here the safety and efficacy of HD and PD in correlation with different mechanisms of post-SG stenosis. Adverse events, technical features of dilation, short and long term follow up were secondary endpoints.

Aims & Methods: Retrospective study conducted in an endoscopic tertiary referral center. All patients presenting with post-SG stenosis and treated by endoscopic balloon dilation were included. Endoscopic treatment consisted in ≥ 1 HD (15-20mm CRE balloon) and/or ≥ 1 PD (30-40mm achalasia balloon). We defined stenosis as "organic" if a narrowing of the digestive lumen due to stapling or fibrosis was evidenced, "functional" in case of

a kink or a twist of SG with preserved flexibility was observed and "combined" if both mechanisms were suspected. Success of endoscopic treatment was defined as complete if all initial symptoms disappeared, partial or absent at 1-month post treatment.

Results: From 2013 to 2019, 44 patients (73% women; mean age 45.5 ± 11 years) underwent an Endotherapy for symptomatic post SG stenosis (15 (34%) and 29 (66%) were treated by HD and PD, respectively) and were followed in our department for a mean period of 22 ± 32 months. Two patients had PD following initial ineffective HD Post-SG stenoses were classified as organic in 10 (23%), functional in 21 (48%) and combined in 13 (29%) patients. Fifteen patients had a history of post-SG leakage which has been healed for a mean time of 22 ± 32 months at the time of the first dilation. Major symptoms at the time of treatment were dysphagia (82%), vomiting (75%), and post-prandial pain (58%). After a mean of 1.8 ± 1.1 dilations, 22 (50%) of patients had a total remission of symptoms and another 20 (total 96%) a partial improvement. At the end of follow up, 80% of patients had no need for additional therapy and no recurrence of post-SG stenosis symptoms. Five patients (11%) underwent another bariatric surgery (3 RYGBP) at the end of follow-up (2 of them for other reasons than those related to post SG stenosis). One perforation occurred after 40 mm PD, successfully treated by surgery, but prompting us to limit further dilations to 35 mm.

Obviously, HD were more frequent in organic stenosis (8/10), while PD were more frequent in functional stenosis (18/21) and in combined stenosis (9/13; $p < 0.001$). Taking into consideration this bias of selection, initial post-dilation success was similar in both type of stenoses. At the end of follow-up significantly more patients with isolated functional stenosis had a persistent improvement compared to patients with organic or combined stenosis (100% vs. 70% vs. 54%; $p = 0.004$). Success of dilation(s) isn't dependent on leakage history or the time between SG and first dilation ($p > 0.05$).

Conclusion: Endoscopic balloon dilation is an effective and safe treatment for post-SG stenosis, the type of which has to be adapted to the anatomical presentation. That being said, when tailoring the type of dilation to the type of stenosis, persistent long-term clinical improvement is observed in 80% of the cases and in almost all patients with functional stenosis.

Disclosure: Nothing to disclose

P1414

SUPERIOR BENEFIT AND SURVIVAL IN OLDER PATIENTS AFTER PALLIATIVE COLONIC STENTING FOR MALIGNANT LARGE BOWEL OBSTRUCTION

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Introduction: Recently updated European Society of Gastrointestinal Endoscopy (ESGE) guidelines have clearly positioned self-expandable metal stents (SEMS) as the preferred management for acute malignant colonic obstruction in patients who are unsuitable for curative surgical resection. We aimed to assess the benefit and survival achieved in older patients who underwent SEMS for palliation in malignant large bowel obstruction, compared to a younger cohort.

Aims & Methods: Patients referred for colonic stenting between 2010 and 2020 were included for analysis. Data was recorded for technical and clinical outcomes, and subsequent progress, including late complications, re-stenting or any required surgery, and time to death. In order to

objectively assess stent benefit and the impact of adverse events, we reported time to re-intervention (re-stenting, surgery or death without re-intervention), and overall survival (death, irrespective of any additional interventions).

Results: 124 patients with palliative obstructing colorectal cancer underwent a primary SEMS procedure, including 29 patients with obstruction proximal to the splenic flexure (23% of total). The median age of patients was 73 years (range 27 - 94 years; 55% male); 58 patients were aged 75 years or over, and 66 patients were aged 74 years or younger. Clinical success in relieving colonic obstruction was similar at 80% versus 86% ($p=0.42$); any technically successful SEMS that failed to fully resolve large bowel obstruction were excluded; there were no procedural perforations.

In 104 patients where SEMS was clinically successful (47 patients $\geq$ 75 years and 57 patients $<$ 75 years), the median survival for older patients was significantly greater at 334 days v 242 days ($p=0.023$). Late complications and the need for further intervention were significantly less common in the ≥ 75 year old group with 4 events v 15 events ($p=0.019$), with 1 stoma v 4 stomas respectively).

Late complications occurred at a median of 204 days (range 27 - 948 days), with the most frequent event being large bowel re-obstruction due to stent overgrowth (11 re-stents and 5 stoma surgeries, and 3 events received no intervention). Therefore the duration of intervention-free benefit was also significantly greater in the ≥ 75 years group at 324 days v 177 days ($p=0.012$).

Conclusion: In our experience, older patients would appear to have a significantly more favourable outcome after SEMS in palliative colorectal cancer, with a longer duration of intervention-free benefit with fewer complications, and longer overall survival. Possible mechanisms might relate to later cancer presentation in younger patients, more indolent tumour biology in older patients, or perhaps a secondary effect from a difference in oncological approach relevant to age.

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Disclosure: Nothing to disclose

P1415

INTENSIVE ENDOSCOPIC THERAPY FOR UNTREATED CERVICAL STRICTURES AFTER ESOPHAGECTOMY: A PILOT STUDY

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Introduction: Development of anastomotic esophageal strictures occurs in up to 43% of patients after esophagectomy with cervical anastomosis.¹ Disease burden is significant due to complaints of dysphagia, need for repeated endoscopic dilation procedures and high risk of recurrence.

Aims & Methods: Our objective was to study the technical feasibility and safety of intensive endoscopic therapy for untreated benign cervical anastomotic strictures after esophagectomy.

In this pilot study, between July 2017 and September 2018 we included 15 patients with a newly diagnosed and untreated benign cervical esophago-gastric anastomotic stricture after esophagectomy. Patients were selected based on an Ogilvie dysphagia score ≥ 2 .² A stricture was defined as the inability to pass with a regular diagnostic gastroscop. Intensive endoscopic therapy included a combination of three endoscopic modalities:

1) at least four longitudinal incisions around the circumference of the stenosis followed by excision of the fibrotic flaps using a needle-knife catheter, allowing the gastroscop to easily pass the stricture.

2) Following in- and excision, a total of 80 mg of triamcinolone was injected into four quadrants of the lesion.

3) After in- and excision and intralesional steroid injections, bougie dilation up to 16 mm was performed. Then the patient was scheduled for a second endoscopic procedure approximately one week later during which bougie dilation up to a luminal diameter of 18 mm was performed.

Patients were followed up to 6 months with monthly evaluation of recurrence of dysphagia, adverse events, general health score from 0 to 100 (= worst to best imaginable health) and therapy satisfaction score from 0 to 10 (= extremely unsatisfied to extremely satisfied).

Results: In 15 patients (9 males, mean age 64.5 years) intensive endoscopic therapy was performed in a single center by one endoscopist after a mean of $78 \pm$ sd (standard deviation) 21 days following esophagectomy. All cervical anastomoses were hand-sewn and 80% (12/15) of patients had experienced postoperative anastomotic leakage which was treated conservatively in all cases. In 60% (9/15) of patients it was feasible to perform at least four incisions around the circumference of the stenosis.

Bougie dilation up to 16 mm during the first and up to 18 mm during the second procedure was achieved in 87% (13/15) and 87% (13/15) of patients respectively. One patient did not undergo the second endoscopic procedure because of a myocardial infarction. Median dysphagia scores significantly improved from 2 (iqr, interquartile range, 2-3) at baseline to 0 (iqr 0-1) after 14 days ($p<0.001$) and 1 (iqr 0-1) after 6 months ($p=0.001$). The mean general health scores did not significantly improve with $62 \pm$ sd 17 at baseline to $69 \pm$ sd 22 after 14 days ($p=0.412$) and $71 \pm$ sd 28 after 6 months ($p=0.313$). The median therapy satisfaction scores after 14 days and 6 months were 9 (iqr 9-10) and 8 (iqr 7-9), respectively. Eleven (73%) patients developed recurrent symptoms of dysphagia for which additional endoscopic bougie dilation was performed.

The median number of endoscopic dilation procedures at 6 months, including the two procedures at baseline, was 3 (iqr 2-5). Adverse events related to the investigational treatment included candida esophagitis ($n=2$, 13%) and pale mucosa / superficial ischemia of the gastric tube after steroid injection ($n=1$, 7%).

Conclusion: Achieving a luminal diameter of 18 mm in two procedures with intensive endoscopic therapy is technically feasible, safe and effective in reducing symptoms of dysphagia.

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Disclosure: Nothing to disclose

P1416

LOCAL ABLATION THERAPY OF COLO-RECTAL PULMONARY METASTASES: A RETROSPECTIVE ANALYSIS OF THE OUTCOME DETERMINANTS

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Introduction: Image-guided percutaneous thermal ablation can be used for treatment of non-operable primary and metastatic lung tumors. These techniques are based on heating effect on the tissue around a percutaneous applicator causing coagulative necrosis of the tumor cells. Microwave ablation (MWA) is a commonly used locoregional interventional procedure in treatment of pulmonary tumors with satisfactory outcome.

Aims & Methods: To evaluate retrospectively the factors affecting the treatment outcome of microwave ablation (MWA) of colorectal lung metastases.

189 patients (average age 60.8 +/- 4.5 years, 90 male & 99 female) with 228 inoperable pulmonary colorectal metastases were included between November 2008 to October 2019; tumor board decision was to perform CT-guided MWA. Initial CT assessment of lesions size, volume, outlines, location in relation to hilum, vascular and bronchial structures followed by CT-guided MWA.

Post-ablation follow-up contrast enhanced CT was performed at 24 hours, 3, 6, 9, 12 months then every 6 months to determine response to treatment. Certain parameters including the pre-ablation size and volume, lesion location in relation to lung hilum, pulmonary vessels or bronchial tree, pathological type and outlines of the lesions are precisely evaluated and correlated with the follow up images and long-term treatment response.

Results: 188 lesions (82.5%) showed complete response with no residual activity while 80 lesions (17.5%) showed incomplete response on follow up. Certain factors have been found and suggested as early predictors for the response including the maximum diameter of the lesion as well as its volume and location in relation to hilum with significantly better response seen with peripherally located lesions less than 3 cm in diameter ($p=0.019, 0.026, 0.037$ respectively). The tumor pathology and location of the lesion as well as its relation the significant vessel or bronchus and outlines of lesions in the current study didn't seem to affect the overall response ($p=0.41, 0.34, 0.47, 0.18$ respectively). 189 patients (average age 60.8 +/- 4.5 years, 90 male & 99 female) with 228 inoperable pulmonary colorectal metastases; tumor board decision was to perform CT-guided MWA. Initial CT assessment of lesions size, volume, outlines, location in relation to hilum, vascular and bronchial structures followed by CT-guided MWA.

Post-ablation follow-up contrast enhanced CT was performed at 24 hours, 3, 6, 9, 12 months then every 6 months to determine response to treatment. Certain parameters including the pre-ablation size and volume, lesion location in relation to lung hilum, pulmonary vessels or bronchial tree, pathological type and outlines of the lesions are precisely evaluated and correlated with the follow up images and long-term treatment response.

Conclusion: Microwave ablation therapy of colorectal lung metastases is a safe effective minimally invasive therapeutic tool with the preablation tumor size, volume and location in relation to lung hilum are the main determinant of the treatment efficacy.

Disclosure: Nothing to disclose

P1417

COMPLICATIONS OF CT-GUIDED MICROWAVE ABLATION OF COLORECTAL PULMONARY METASTASES: A RETROSPECTIVE RISK ANALYSIS

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Introduction: Microwave ablation (MWA) is a commonly used locoregional interventional procedure in treatment of pulmonary tumors with satisfactory outcome. Certain complication can occur during MWA of lung tumors, the most common complications encountered are pneumothorax and pulmonary hemorrhage. Some risk factors are associated with increased incidence of MWA complications.

Aims & Methods: To evaluate the factors influencing the incidence of complications after microwave ablation (MWA) of colorectal lung metastases. 189 patients (average age 60.8 +/- 4.5 years, 90 male & 99 female) with 228 inoperable pulmonary colorectal metastases were included between November 2008 to October 2019; tumor board decision was to perform CT-guided MWA. Initial CT assessment of lesions size, location, and underlying lung disease followed by CT-guided MWA. The ablation track length traversing aerated lung is measured and whether the microwave antenna is seen traversing pulmonary vessels is then judged. The prevalence of complication was determined, the forementioned parameters are correlated with incidence of complication during the ablation procedure or after it during follow-up period by CT at 24 hours, 3, 6, 9, 12 months post-ablation. The complications were adequately managed.

Results: 63 ablation session of (27.6%) of patients had complications with pneumothorax is most common complication seen 24 session (10.5 %) 16 cases were managed conservatively, 6 cases with manual evacuation and 2 cases needed intercostal tube insertion. Pulmonary hemorrhage in 19 session (8.3 %). Pleural effusion seen in 11 cases (3.1 %), hemoptysis seen 3 cases (1.3 %), post-ablation syndrome seen in 3 cases (1.3 %) and skin burn in 1 case (0.4 %), surgical emphysema in 1 cases, 0.4 %, pulmonary infection in 1 case, 0.4 %. No deaths during procedure. Significant risk factors associated with development of pneumothorax were:

- Patient above 60 years ($p=0.027$),
- comorbid emphysema ($p=0.041$),
- Tumor size < 3 cm ($p=0.016$),
- lower lung lesions ($p=0.045$),
- Traversing aerated lung parenchyma in the needle track for a distance > 2.6 cm ($p=0.018$), and;
- traversing a major pulmonary fissure ($p=0.036$).

Significant risk factors associated with pulmonary hemorrhage were:

- tumor size < 3 cm ($p=0.017$),
- lower lung lesions ($p=0.023$),
- traversing aerated lung parenchyma in the needle track for a distance > 2.6 cm ($p=0.011$), and;
- traversing pulmonary vessels by the ablation needle ($p=0.013$). Peripheral subpleural lesion associated with pleural effusion ($p=0.01$).

Conclusion: Microwave ablation therapy is a relatively safe effective treatment for colorectal lung metastases with spectrum of complications, certain factors increase the risk of associated complication as lesion size, location, needle track passing through lung together with comorbid lung disease as emphysema.

Disclosure: Nothing to disclose

Poster presentations

Surgery

Surgery

09:00-19:00 / Poster Exhibition

P1418

HISTOLOGICAL GRADING EVALUATION OF NON-ALCOHOLIC FATTY LIVER DISEASE AFTER BARIATRIC SURGERY: A RETROSPECTIVE AND PROSPECTIVE OBSERVATIONAL COHORT STUDY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a chronic disease with several degrees of histological features which may progress to cirrhosis. Obesity is an important risk factor and although NAFLD has no specific pharmacological treatment, bariatric surgery has been associated with NAFLD regression in severely obese patients. However, few longitudinal histological studies support this finding.

Aims & Methods: This study aimed to characterize the NAFLD of obese Brazilian patients and to analyze the histologic evolution throughout the spectrum of NAFLD, while assessing the effects of bariatric surgery on the attenuation of this liver disease. Firstly, a retrospective study was performed including clinical and histological data of 895 obese patients who underwent Roux-en-Y Gastric Bypass (RYGB) surgery. In addition, histological analyses of 30 patient's liver biopsies were evaluated at two time-points (T1 and T2). All procedures were in accordance with the Declaration of Helsinki and the Ethics Committee from the University of Campinas approved the study.

Results: The retrospective analysis of the total number of patients revealed that the average body mass index (BMI) was 35.91 ± 2.81 kg/m². Of all patients, 306 (34%) had normal serum levels of all blood tests, while 589 (66%) exhibited at least one altered serum levels when compared to the reference values of each test - as born out by 35% of the glucose, 21% of alanine aminotransferase, 13% of the gamma glutamyl transferase, 10% of the total bilirubin, 9% of the total protein, 9% of the aspartate aminotransferase, 2% of the alkaline phosphatase and 1% of the plasma albumin blood tests. In addition, the serum glucose level of 66 patients (7,3% of all patients) was equal to or greater than 126 mg/dl, which is considered diabetic. The liver biopsies during bariatric surgery showed that 51.51% did not present NAFLD, 37.99% had NASH, 10.17% isolated steatosis and 0.33% liver cirrhosis. The median BMI of the longitudinal cohort decreased from 37.9 ± 2.21 kg/m² at the time of bariatric surgery (T1) to 25.7 ± 3.79 kg/m² after 21 ± 22 months after the procedure (T2).

At the time of their bariatric surgery, 23 (77%) of the obese patients presented abnormal levels compared to the reference values. The prevalence of NAFLD in T1 was 50%, and 16.67% in T2. The histological area of collagen fiber (Masson's Trichrome staining) was lower in T2 compared to T1 ($p=0.0152$), besides no difference of T2 to the control group ($p>0.05$), corroborating the NAFLD regression that occurred in the majority of obese

patients after bariatric surgery in this cohort. These results was also illustrated by immunohistochemistry for Kupffer cell and myofibroblast formation markers.

Conclusion: These findings confirmed the NAFLD regression after bariatric surgery and, for the first time, showed the amelioration of these features using more accurate histopathological techniques.

References: 1. Huang, T.D., Behary, J., Zekry, A. Non-alcoholic fatty liver disease (NAFLD): a review of epidemiology, risk factors, diagnosis and management. Intern. Med. J. doi:10.1111/imj.14709 (2019). 2. Coccia, F., et al. Insulin resistance, but not insulin response, during oral glucose tolerance test (OGTT) is associated to worse histological outcome in obese NAFLD. Nutr. Metab. Cardiovasc. Dis. 30(1), 106-113 (2020). 3. Younossi, Z.M., Marchesini, G., Pinto-Cortez, H., Petta, S. Epidemiology of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: implications for liver transplantation. Transplantation. 103(1), 22-27 (2019). 4. Bedossa, P., et al. Histopathological algorithm and scoring system for evaluation of liver lesions in morbidly obese patients. Hepatology. 56(5), 1751-1759 (2012). 5. Younossi, Z., et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat. Rev. Gastroenterol. Hepatol. 15(1), 11-20 (2018).

Disclosure: Nothing to disclose

P1419

THE NATURAL COURSE OF GIANT PARAESOPHAGEAL HERNIA AND LONG-TERM OUTCOMES FOLLOWING CONSERVATIVE MANAGEMENT

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Introduction: A giant paraesophageal hernia can present itself in a wide variety of forms, ranging from an incidentally detected hernia without symptoms, to a gastric volvulus with risk of ischemia. The management of asymptomatic or mildly symptomatic patients has been widely debated for decades. Due to a paucity of cohort studies, accurate information on the natural course of paraesophageal hernia is scarce, challenging therapeutic decisions whether or not to operate.

Aims & Methods: We aimed to investigate the long-term outcomes of patients with a giant paraesophageal hernia and to determine factors associated with clinical outcome. We retrospectively analyzed charts of patients diagnosed with giant paraesophageal hernia between January 1990 and August 2019, collected from a university hospital in the Netherlands. Included patients were subdivided into three groups based upon primary therapeutic decision at diagnosis. Radiologic, clinical, and surgical characteristics, along with long-term outcomes at most recent follow-up, were collected.

Results: We included 293 patients (91 males, mean age 70.3 ± 12.4 years) with a mean duration of follow-up of 64.0 ± 58.8 months. Of the 220 patients that were conservatively treated, a total hernia-related mortality of 1.5% was observed. Hernia-related complications, varying from uncomplicated volvulus to strangulation, occurred in 8.1% patients. Only 1.1%

of patients included in this study required emergency surgery. Logistic regression analysis revealed presence of symptoms (odds ratio (OR)=4.44 95% confidence interval (CI)=1.79-20.62), in particular obstructive symptoms (vomiting, OR=15.7, 95% CI=4.60-53.57; epigastric pain, OR=4.37, 95% CI=1.21-15.76), and Cameron lesions on endoscopy (OR=17.0, 95% CI=1.33-216.67) to be associated with occurrence of hernia-related complications.

Conclusion: Hernia-related death and morbidity is low in conservatively treated patients. Therefore, conservative therapy is an appropriate therapeutic strategy for asymptomatic or mildly symptomatic patients.

Disclosure: Nothing to disclose

P1420

OUTCOMES OF LAPAROSCOPIC REPAIR FOR INTRATHORACIC STOMACH IN JAPANESE COHORT

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Introduction: Intrathoracic stomach (ITS) is a relatively rare foregut disorder characterized by herniation of most of the stomach into the posterior mediastinum. Higher recurrent rate after surgical repair of ITS has been reported and this disease is therefore considered to be more clinically challenging. The number of patients with ITS in Japan is expected to increase due to population aging fast; however, the clinical data from this country is scarce. The aim of this study is to assess the outcomes of laparoscopic repair for ITS among Japanese cohort.

Aims & Methods: The aim of this study is to assess the outcomes of laparoscopic repair for ITS among Japanese cohort.

Patients who underwent primary antireflux surgery at our hospital between May 2007 and July 2019 were included. All antireflux procedures were laparoscopically approached. Patients were divided into two groups; ITS group or non-ITS group. ITS was defined as >50% of the stomach within the thoracic cavity.

Each patient postoperatively rated oneself with a satisfaction score on a scale of 1 (unsatisfied) to 5 (satisfied). Endoscopic surveillance was conducted at 3 months, 1 year, and then yearly after antireflux surgery. Kaplan-Meier analysis was performed to assess cumulative probability of post-operative esophagitis and recurrent hiatal hernia.

Results: A total of 318 patients underwent laparoscopic antireflux procedure during the study period. 52 patients (16.4%) were diagnosed with ITS and 266 patients (83.6%) were with non-ITS. The ITS group was older, female-dominant, and had similar BMI compared with the non-ITS group (75 vs. 53 years, $p<0.001$; 73.1% vs. 34.6%, $p<0.001$; 23.4 vs. 24.0 kg/m², $p=0.295$, respectively). Median follow-up periods after surgery were 22.0 months in the ITS group and 16.0 months in the non-ITS group ($p=1.000$). Gastric volvulus was seen in 69.2% of the ITS patients (36/52 patients). Dysphagia was more common in the ITS group than in the non-ITS group (42.3% vs. 7.5%, $p<0.001$), while lower rate of preoperative esophagitis was evident in the ITS group (27.3% vs. 52.0%, $p=0.008$).

Most of the patients in both groups underwent Toupet fundoplication (ITS 94.2% vs. non-ITS 95.5%, $p=0.456$). Mesh crural reinforcement and/or gastropexy were more frequently performed in the ITS group than in the non-ITS group (73.1% vs. 26.7%, $p<0.001$; 30.8% vs. 3.0%, $p<0.001$, respectively). Patients in the ITS group had longer operative time and higher incidence of intraoperative complications (220 vs. 144 minutes, $p<0.001$; 23.1% vs. 6.4%, $p=0.001$); however, both groups showed good to excellent

clinical satisfaction (4-5 points, 83.3% vs. 89.7%, $p=0.237$). Kaplan-Meier analysis illustrated that the incidence of 1-, 2-, and 3-years postoperative esophagitis were comparable between the groups (0, 3.7, and 3.7% vs. 1.9, 5.8, and 5.8%, log-rank test $p=0.952$), although those of recurrent hiatal hernia were higher in the ITS group (12.0, 19.2, and 19.2% vs. 0.8, 2.7, and 5.2%, log-rank test $p=0.003$).

Conclusion: Good clinical satisfaction can be expected after laparoscopic repair for ITS. Incidence of recurrent hiatal hernia was high, which signifies requirement to improve treatment strategy.

Disclosure: Nothing to disclose

P1421

CHEMORADIO THERAPY FOLLOWED BY ACTIVE SURVEILLANCE VERSUS SURGERY FOR OESOPHAGEAL CANCER: A SYSTEMATIC REVIEW AND INDIVIDUAL PATIENT DATA META-ANALYSIS

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Introduction: Up to 50% of patients with oesophageal cancer have a pathologically complete response after neoadjuvant chemoradiotherapy (nCRT) plus surgery. An active surveillance strategy may be feasible in patients with a complete clinical response (cCR) after nCRT.

The aim of this study was to perform a meta-analysis using data of individual patients that underwent active surveillance with surgery for recurrent disease versus standard surgery after nCRT.

Aims & Methods: A systematic search was performed in Embase, Medline, Web of Science, Scopus and Cochrane until February 12, 2020 and the study protocol was prospectively registered in PROSPERO (CRD42020167070). Studies were sought including patients with cCR after nCRT who underwent active surveillance or standard oesophagectomy and reported on overall survival. Included studies were assessed for risk of bias using Cochrane's tools. Authors were contacted to supply individual patient data. Overall survival and progression free survival were compared using random effects meta-analysis of propensity score matched or randomised data. An additional per-protocol sensitivity analysis was performed for overall survival. Subgroup survival analyses were performed according to histological subtypes. Cumulative incidence of locoregional recurrence was assessed in patients undergoing active surveillance.

Results: All approached authors provided anonymised patient data. Seven studies comprising 788 patients with cCR were identified of which 453 patients were included after propensity score matching or randomisation (196 active surveillance and 257 standard oesophagectomy). Hazard Ratio (HR) for all-cause mortality for active surveillance was 1.08 (95% Confidence Interval (CI): 0.62 - 1.87, $p = 0.75$) after inclusion of all patients and 0.93 (0.56 - 1.54, $p = 0.75$) after per-protocol analysis. HR for progression or all-cause mortality for active surveillance was 1.14 (95% CI: 0.83 - 1.58,

$p = 0.36$). Locoregional recurrence after initial complete clinical response in patients undergoing active surveillance was 34% at two years (95%CI: 21% - 50%) and 40% at five years (95%CI: 26% - 59%).

Conclusion: Overall survival and progression free survival are comparable between patients undergoing active surveillance compared to standard surgery after neoadjuvant chemoradiation. Locoregional recurrences rarely develop after two years of active surveillance. Although these data support an active surveillance strategy, randomized trials have to be completed before an active surveillance strategy can be actively proposed to patients with oesophageal cancer.

Disclosure: Nothing to disclose

P1422

PLASMA FGF-19 AND FGF-21 LEVELS IN NON-RESPONDERS AFTER ROUX-EN-Y GASTRIC BYPASS

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Introduction: Endocrine subfamily members of fibroblast growth factors are broadly considered to be associated with metabolic homeostasis. Specifically, FGF-19 is produced in the gut and regulates bile acid synthesis. FGF-19 has been reported to be decreased in obesity, increasing to normal levels following Roux-en-Y gastric bypass surgery (RYGBP). FGF-21 is a hepatokine associated with sweet tooth behavior, acting through receptors at the paraventricular nucleus of the hypothalamus. It also selectively drives glucose uptake in adipocytes. Plasma level of FGF-21 is positively associated with obesity, BMI and type 2 diabetes.

Aims & Methods: The primary aim of this study was to compare plasma FGF-19 and FGF-21 levels between non-responders and weight responders after RYGBP. Female subjects operated with RYGBP were grouped as non-responders ($n=22$, 26.0 ± 15.9 percent of excess BMI loss, %EBMIL) and weight responders ($n=18$, 74.9 ± 18.2 %EBMIL) according to their weight result five years after surgery.

Groups were matched for preoperative age and BMI as well as follow-up years. Plasma FGF-19 and FGF-21 were measured by ELISA (RnD Systems, Cat DF1900 & DF2100). Glucose homeostasis was assessed by oral glucose tolerance test (OGTT). Blood was sampled at 0 (fasted), 30, 60, 90 and 120 min.

Comparisons were made between non-responders and weight responders, as well as with a healthy fasted non-operated reference. In a subgroup analysis, differences between type 2 diabetes mellitus (T2DM) and normoglycemic subjects were also studied.

Results: FGF-19 healthy fasted reference QC was 315 ng/L. No RYGBP subjects reached this level during OGTT, going from 60 ± 47 ng/L (median $\pm$ SD) to peak of 78 ± 53 ng/L at 90 min. No differences were seen in FGF-19 between RYGBP groups. FGF-21 of healthy fasted reference QC was 67 ng/L. Most RYGBP subjects were far above this, with FGF-21 of 413 ± 823 ng/L at OGTT baseline to peak at 120 min (442 ± 611). Non-responders had significantly higher FGF-21 at 90 min than weight responders. T2DM subjects had significantly higher FGF-21 at 60 min than normoglycemic subjects.

Conclusion: Several years after RYGBP, FGF-19 is lower and FGF-21 is higher than the healthy reference. Non-responders and T2DM subjects can be differentiated from responders. Non-responders tend to experience FGF-21 plasma concentration that is particularly elevated in the cardinal time window in OGTT when glucose and insulin are highest. Elevated FGF-21

could conceivably underlie exaggerated sweet tooth behavior and selective glucose deposition to adipose tissue in non-responders.

Disclosure: Nothing to disclose

P1423 WITHDRAWN

P1424

DEVELOPMENTS IN THE SURGICAL TREATMENT OF ACUTE APPENDICITIS - A GERMANY-WIDE, POPULATION-BASED STUDY

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Introduction: Appendectomy is considered to be the gold standard treatment for acute appendicitis. However, particularly in acute uncomplicated appendicitis, surgical treatment has been questioned in various randomised controlled trials advocating antibiotic first-line treatment [1, 2].

Aims & Methods: The aim of this study was to present the current developments in the surgical treatment of the disease with special consideration of the sub-classification into acute uncomplicated and complicated appendicitis. For this population-based observational study, standardised hospital discharge data (Diagnosis-Related Groups statistics) were used to analyse developments, in-hospital mortality and morbidity in the treatment of acute appendicitis in Germany from 2010 to 2017.

All patients in Germany who received appendectomy for acute appendicitis were included. Calculations were performed with SAS Version 9.3 (SAS Institute Inc., Cary, NC, USA).

The data were analysed descriptively for each year and are expressed as absolute and relative numbers. In addition, in-hospital mortality and indicators of a complicated clinical course in acute appendicitis were further investigated.

Results: In total, 865,688 patients were analysed. The number of appendectomies per year showed a relative decrease of 9.8% (113,614 in 2010 compared to 102,464 cases in 2017), caused by a decreasing proportion of operations for uncomplicated appendicitis (82% in 2010 compared to 78% in 2017).

In contrast, the number of operations for complicated appendicitis increased from 18% ($n = 20,479$) to 22% ($n = 22,558$). The in-hospital mortality rate for the entire study population was 0.12% in 2017, compared to 0.16% in 2010.

Further, a substantial decrease of the in-hospital mortality from 5.4% in 2010 to 3.4% in 2017 was observed in cases with a complicated course.

Conclusion: The results show that in recent years the therapeutic strategies for acute appendicitis in Germany have been influenced by current evidence in favour of a primarily non-surgical approach in selected patients. Treatment outcomes with respect to in-hospital mortality have improved over the same period, suggesting improved surgical care. Noteworthy, although the in-hospital mortality in patients with a complicated courses of the disease was considerably higher, it declined during the study period, as well.

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cillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *Lancet*, 2011. 377(9777): p. 1573-9.

Disclosure: Nothing to disclose

P1425

ROUTINE HISTOPATHOLOGICAL EXAMINATION FOLLOWING APPENDECTOMY IS UNNECESSARY: RESULTS OF THE MULTICENTRE PROSPECTIVE FANCY STUDY

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Introduction: Due to significant costs and increased workload of pathologists, the necessity of routine histopathological examination following appendectomy has been questioned for several decades. The debate remains ongoing as prospective studies investigating a selective policy and its oncological safety are lacking.

Aims & Methods: This multicentre prospective study aimed to determine whether selective histopathological examination of appendectomy specimens following macroscopic examination by the surgeon is oncologically safe. For a period of nine months, all appendices removed for suspected appendicitis were systematically assessed by surgeons in 59 Dutch hospitals.

Following visual inspection and digital palpation, the surgeon reported whether macroscopic abnormalities suspicious for an appendiceal neoplasm were present, and if further microscopic assessment by the pathologist was indicated. Subsequently, all specimens were sent for histopathological examination. The primary outcome was oncological safety of selective histopathological examination, assessed by calculating the number of patients in whom an appendiceal neoplasm with clinical consequences benefitting the patient would have been missed.

The following consequences were considered beneficial: presence of residual disease in the re-resection specimen, treatment with chemo-, radio- or immunotherapy, palliative care for metastases detected during staging procedures, and diagnosis of serrated polyposis syndrome or removal of (pre)malignant lesion(s) during colonoscopy.

If an additional resection was performed and no residual disease was found, this was considered harmful due to the unnecessary surgical risks the patient was exposed to. A selective policy was considered safe if, within the group of specimens that would not have been sent for histopathological examination, the upper limit of the two-sided 95% con-

fidence interval of the proportion of missed appendiceal neoplasms with clinical consequences benefitting the patient was below 3 per 1000 specimens.

Results: A total of 7339 patients were included, of whom 130 (1.77%) were diagnosed with an appendiceal neoplasm. Surgeons considered that histopathological examination was not indicated in 4966 (67.7%) patients. Of these, 59 (1.19%) were diagnosed with an appendiceal neoplasm (neuroendocrine tumor, n=28; non-invasive epithelial neoplasm, n=22; invasive epithelial neoplasm, n=9). The diagnosis had clinical consequences for 22 patients. These were considered beneficial in five patients, in whom residual disease was radically removed. This implies that in a hypothetical situation of selective histopathological examination, the diagnosis of an appendiceal neoplasm with clinical consequences benefitting the patient would have been missed in 1.01 per 1000 patients (upper limit 95% CI 1.61 per 1000 patients). Ten patients experienced harm, as they underwent an additional resection without residual disease found in the re-resection specimen. Consequences were neither beneficial nor harmful for five patients who only underwent diagnostic tests without further treatment and two patients who were subjected to follow-up.

Conclusion: Routine histopathological examination of appendectomy specimens is unnecessary and seems even harmful rather than beneficial. A selective policy following macroscopic examination by the surgeon is oncologically safe and will likely result in a reduction of costs, pathologists' workload and unnecessary additional resections.

Disclosure: This investigator initiated study was supported by the Netherlands Organisation for Health Research and Development (ZonMw) under grant number 843002822, of which the Dutch Ministry of Health, Welfare and Sports and the Dutch Organisation for Scientific Research are the main commissioning organisations. ZonMw has not played a role in designing the study and data collection, nor has it influenced the analysis and writing process of the abstract or manuscript.

P1426

IMPACT OF ENHANCED RECOVERY AFTER SURGERY (ERAS) PROGRAM IN PATIENTS WHO UNDERWENT COLORECTAL CANCER SURGERY: A RANDOMIZED CONTROLLED TRIAL STUDY

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Introduction: ERAS programs in colorectal surgery are widespread and broadly accepted. Successful implementation of these programs are challenging based on their compliance due to existing barriers. ERAS failure was recently reported to mostly related to a prolonged postoperative length-of-stay (poLOS).

The objectives of this study are to compare between ERAS and traditional programs in the poLOS, postoperative complications, and rate of revisit within 30 days after discharge. Subgroup analysis was performed to determine the association between mechanical bowel preparation (MBP) and outcomes of surgery.

Aims & Methods: In general, ERAS guidelines for elective colon surgery include 21 items. In ERAS program, patients were had nothing per oral (NPO) after 3 AM and no mechanical bowel preparation. In traditional program, patients were fasted after midnight and received mechanical bowel preparation with polyethylene glycol 2 liters or sodium phosphate 90 milliliters.

Both groups were received prophylaxis antibiotic 30 min before incision. Intraoperative period, traditional group were received general anesthesia while ERAS group were received combined general and epidural at T7-8

level anesthesia. Postoperative period, patients in the traditional group were had NPO for 3-5 days and control pain with strong opioid. In ERAS group, the patients were started with liquid diet within twenty-four hours, patients were encouraged to ambulate within six hours after surgery and control pain with epidural anesthesia and paracetamol. Weak opioid was given when pain score was greater than or equal to four.

Results: Forty-six patients were included, 22 and 24 patients were randomized to traditional and ERAS groups, respectively. Average age was 62 ± 8.17 and 63 ± 9.05 years old in traditional and ERAS groups, respectively. The median postoperative poLOSs were 8 (7-9) and 6 (5-6.5) days in traditional and ERAS groups, respectively ($p < 0.0001$).

Postoperative complications were surgical site infection and ileus in 4.55 vs 4.17% ($p = 1.000$), and 4.55 vs 0% ($p = 0.478$) in traditional and ERAS group, respectively.

Postoperative pain score in 24 and 48 hours were 2.5 (2-4) vs 2 (2-2), ($p = 0.170$) and 3 (3-4) vs 2 (1-2), ($p < 0.001$) in traditional and ERAS group, respectively. In subgroup analysis, there was no significant different in outcomes of surgery in patients who had MBP.

Conclusion: Despite the proven benefits of ERAS programs in colorectal surgery, our study confirms the important of poLOS in the successful application of protocol. There was no difference between MBP vs no preparation.

Disclosure: Nothing to disclose

P1427

PANCREATO-BILIARY MANIFESTATIONS OF NON-ALCOHOLIC FATTY LIVER DISEASE: A CASE-CONTROL MULTI-CENTER STUDY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) has become a major cause of chronic liver disease. Several extrahepatic manifestations have been reported in relation to NAFLD. However, data regarding pancreato-biliary manifestation are scarce.

Aims & Methods: We aimed to explore the association of pancreato-biliary manifestations with NAFLD. A retrospective multi-center study that included all patients who underwent an endoscopic ultrasound (EUS) performed for hepatobiliary indications and for whom the endosonographer reported on the presence or absence of fatty liver. The EUS reports were reviewed and all pathological findings were reported.

Results: Overall, 545 patients were included in the study, among them, 278 patients had fatty liver (group A) as compared to 267 who didn't have (group B). The average age in group A was 64.5 ± 13.5 years vs. 61.2 ± 14.7 years in group B. Male gender constituted 49.6% and 58% in groups A and B, respectively.

On multivariate analysis, fatty pancreas (OR 4.02, $P = 0.001$), serous cystadenoma (SCA) (OR 5.1, $P = 0.0009$), mucinous cystadenoma (MCA) (OR 9.7, $P = 0.005$), side-branch intraductal papillary mucinous neoplasm (IPMN) (OR 2.76, $P < 0.0001$), mixed-type IPMN (OR 16.4, $P = 0.0004$), pancreatic neuroendocrine tumor (NET) (OR 8.76, $P < 0.0001$), gallbladder stones (OR 1.9, $P = 0.02$) and hilar lymphadenopathy (OR 6.8, $P < 0.0001$) were significantly higher among patients with NAFLD.

After adjustment for fatty pancreas, the association remained significant for SCA (OR 3, $P = 0.01$), MCA (OR 4.6, $P = 0.03$), side-branch IPMN (OR 1.7, $P = 0.02$), mixed-type IPMN (OR 5.5, $P = 0.01$) and pancreatic NET (OR 4.5, $P = 0.001$).

Conclusion: Pancreato-biliary manifestations are common among patients with NAFLD. Assessment of these coexistent manifestations should be considered in the setting of NAFLD patients.

Disclosure: Nothing to disclose

P1428

A DUTCH PREDICTION TOOL TO ASSESS THE RISK OF INCIDENTAL GALLBLADDER CANCERS IN CHOLECYSTECTOMIES FOR BENIGN GALLSTONE DISEASE

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Introduction: A selective histopathologic (Sel-HP) policy of gallbladder specimens following cholecystectomy is increasingly implemented in low incidence countries. However, the fear of missing incidental gallbladder cancer (iGBC) persists and thereby restrict further implementation of a Sel-HP policy. This study aims to develop a diagnostic prediction model for selecting gallbladders in need of histopathologic examination after cholecystectomy.

Aims & Methods: A registration based retrospective cohort study of nine hospitals in the Southern part of the Netherlands between January 2004 and December 2014 was used. Data was collected using a secure linking of 3 patient databases (nationwide network and registry of histo- and cytopathology in the Netherlands, Netherlands Cancer Registry and Dutch Hospital Database). Four potential clinical predictors for gallbladder cancer (GBC) were selected based on previous literature and expert opinion. The prediction model was internally validated by bootstrapping. Discriminative capacity and accuracy were tested by assessing the area under the receiver operating characteristic curve (AUC) and visual inspection of a calibration plot. Finally, a clinical 4-step protocol was formulated using radiological, clinical indications correlated with high susceptibility for GBC development, macroscopic examination of the gallbladder and finally the clinical prediction model.

Results: The prediction model was developed using a cohort of 31902 gallbladders containing 109 GBC cases. A model was developed including the following variables: age, sex, type of surgery and indication for surgery. The AUC was 81.7% (95% confidence interval 77.7% - 85.7%), indicating a good discriminative ability of the model. The calibration plot indicated good calibration of the predicted probabilities.

Conclusion: We developed a clinical prediction model for selecting gallbladder specimens for histopathologic examination after cholecystectomy for ruling out GBC. This protocol will support surgeons in selecting appropriate gallbladders specimens for selective pathologic policy.

Disclosure: Nothing to disclose

P1429 WITHDRAWN

P1430

DEVELOPMENT AND VALIDATION OF A PREDICTION MODEL TO SELECT PATIENTS WITH SYMPTOMATIC CHOLECYSTOLITHIASIS FOR CHOLECYSTECTOMY - A PROSPECTIVE, MULTICENTRE STUDY

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Introduction: Within our medical community, there is no consensus on the indication for surgery in patients with uncomplicated gallstones disease.

Aims & Methods: This study determines the value of the current Rome criteria to predict patient-reported outcomes. Secondly, we report the development and validation of a prediction model to better select for surgery. We included patients with symptomatic, uncomplicated cholecystolithiasis in two multicentre, prospective trials. First, we assessed the value of the Rome criteria to predict a pain-free state after surgery, absence of biliary colic, and a clinically relevant pain reduction. Second, we used a multivariable logistic regression analysis to develop a model to predict a clinically relevant pain reduction after surgery. Area under the receiver operating curve (AUC) is used to express model performance. Internal and external validation was performed.

Results: In total, 1561 patients were included, 494 patients in the derivation cohort, and 1067 patients in the validation cohort. In the derivation cohort, 80.0% of patients underwent cholecystectomy. After cholecystectomy, 57.0% of patients was pain-free, 95.2% reported absence of biliary colic, and 79.9% reported a clinically relevant pain reduction. The Rome criteria poorly predicted a pain-free state, absence of biliary colic, or clinically relevant pain reduction (AUC 0.56, 0.58, and 0.60 respectively). Our final prediction model showed that male patients, no history of abdominal surgery, an increased VAS baseline score, pain in attacks, pain-radiation to the back, pain-reduction with simple analgesics, and no heart burn are independent factors predicting a clinically relevant post-operative pain reduction. Internal and external validation of this model showed an AUC 0.75 (95% CI 0.68-0.81), and 0.64 (95% CI 0.58-0.70), respectively.

Conclusion: Current Rome criteria poorly select patients for cholecystectomy. The present model is a first step to accurately predict outcome after cholecystectomy. This aids clinicians to better select future patients for surgery.

Disclosure: Nothing to disclose

P1431

THE INFLUENCE OF PEROPERATIVE LIVER TEXTURE ON SHORT TERM SURGICAL MORBIDITY AND MORTALITY IN PATIENTS UNDERGOING HEPATECTOMY FOR BENIGN CONDITIONS: A NSQIP DATA ANALYSIS

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Introduction: Liver resection is performed as a primary treatment option for benign hepatic lesions. We aim to investigate the correlation between the liver texture described during hepatectomy for benign lesions and the 30-day post-operative outcomes.

Aims & Methods: We studied all patients undergoing hepatectomy from the National Surgery Quality Improvement Program (NSQIP) database. NSQIP includes prospective validated outcomes and anonymized data for patients' demographics, functional statuses, preoperative risk factors, laboratory data, and 30-day postoperative outcomes for patients undergoing major surgery in more than 500 hospitals. Descriptive statistics were presented as % for categorical variables and mean $\pm$ SD for continuous variables. Bivariate analysis was conducted to check for correlation between postoperative outcomes and the liver texture. A p-value of 0.05 was considered statistically significant.

Liver texture	Normal Liver (4411)	Fatty (1935)	Cirrhotic (1571)	Congested (296)	Total (8231)	p-value
Invasive	325 (7.4%)	167 (8.7%)	145 (9.3%)	39 (13.2%)	676 (8.23%)	0.001
Bile leakage	306 (7.05)	126 (6.6%)	84 (5.4%)	32 (10.9%)	548 (6.67%)	0.0045
Mortality	46 (1.04%)	28 (1.5%)	46 (2.9%)	7 (2.4%)	127 (1.55%)	<0.0001
Wound	302 (6.9%)	156 (8.1%)	106 (6.85)	38 (12.85)	602 (7.3%)	0.0007
Cardiac	43 (1.0%)	26 (1.3%)	34 (2.2%)	5 (1.7%)	108 (1.3%)	0.0046
Respiratory	166 (3.8%)	121 (6.3%)	134 (8.5%)	26 (8.8%)	447 (5.4%)	<0.0001
Urinary	54 (1.2%)	35 (1.8%)	51 (3.3%)	6 (2.0%)	146 (1.8%)	<0.0001
Thrombo-embolism	114 (2.65)	55 (2.8%)	44 (2.8%)	12 (4.1%)	225 (2.7%)	0.49
Sepsis	197 (4.5%)	100 (5.2%)	100 (6.4%)	27 (9.1%)	424 (5.2%)	0.0003
Bleeding	630 (14.3%)	378 (19.5%)	295 (18.85)	92 (31.1%)	1395 (17.05)	<0.0001
Return to OR	98 (2.2%)	58 (3.0%)	55 (3.5%)	13 (4.4%)	224 (2.7%)	0.0097
Composite morbidity	575 (13.0%)	307 (15.9%)	285 (18.1%)	61 (20.6%)	1228 (15.0%)	<0.0001
Readmission related	340 (7.7%)	153 (7.95)	141 (9.0%)	45 (15.2%)	679 (8.3%)	<0.0001
Mean Total operation time	241.4 (118.0)	257.1 (124.2)	220.5 (114.6)	294.0 (137.3)	243.0 (119.6)	<0.0001
Mean Total length of hospital stay	6.4 (6.1)	7.0 (6.9)	7.3 (7.5)	9 (9.4)	6.8 (6.7)	<0.0001

[Table. Comparing 30-day outcomes among patients who underwent hepatectomy according to the liver texture described during the operative procedure]

Results: 8231 patients undergoing hepatectomy were analyzed according to the liver texture described during the operative procedure. Around 53% (4411) of the patients had a normal-appearing liver. 23% (1935) had a fatty appearance, 19% (1571) had cirrhotic changes, and 3% (296) were de-

scribed as congested. When comparing the four described liver textures, “cirrhotic” appearance had the highest mortality risk of 2.9%, followed by “congested” (2.4%), “fatty” (1.5%), and “normal” (1.04%). Cardiac events and urinary infections were highest in the “cirrhotic” group. The rest of the described post-operative complications were highest in the “congested” group and included bile leakage, wound infection, respiratory events, sepsis, bleeding, return to operation, readmissions, the mean total operation time, and the length of hospital stay. The risk of thromboembolism appeared to be highest in the “congested”, however, that difference is not statistically significant between the four groups.

Conclusion: Texture of the liver appears to be a predictive marker for post-hepatectomy 30-day mortality and morbidity for benign liver conditions. Cirrhotic patients appear to have the highest post-operative mortality risk, in addition to post-operative cardiac and urinary complications. Patients with congested liver appear to have the highest overall composite morbidity risk. The risk of thromboembolism did not differ according to liver texture. This study sheds the light on the importance of documenting the texture of the liver during hepatectomy procedures and for possibly incorporating this factor in future complication risk calculations.

Disclosure: Nothing to disclose

P1432

POST-OPERATIVE OUTCOMES FOLLOWING INGUINAL HERNIA REPAIR IN IBD PATIENTS COMPARED TO MATCHED CONTROLS - A CASE CONTROL STUDY

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Introduction: Patients with inflammatory bowel disease frequently undergo gastrointestinal surgical interventions, but only limited data exist surgical outcomes when IBD patients undergo other interventions.

The aim of this study was to assess surgical outcome in IBD patients who underwent inguinal hernia repair and to assess possible risk factors.

Aims & Methods: A retrospective analysis of a prospective database including all IBD patients treated in a large tertiary center between 2008 and 2019 was conducted. IBD patients who underwent inguinal hernia surgery were matched based on demographic characteristics. Clinical operative data was extracted from medical records and analyzed.

Results: Overall, out of 5467 IBD patients treated in our institute, twenty-six patients (0.47%) underwent inguinal hernia repair surgery during the study period. 76 patients match control patients with similar characteristics were compared to the IBD group. Post-operative complications were found to be more common in the IBD group (30.7% vs 11.8%; p=0.03) compared to controls. In addition, higher rates of intra-operative complications (11.5% vs. 3.9%; p=0.17) were seen between the two groups, but without statistical significance. We found no significant differences in Length of stay (3.38 days vs. 2.83; p=0.21), hernia recurrence rate (7.6% vs. 9.2%; p=1) and mean follow up (934 days vs. 820 days; p=0.62).

Within the IBD group, Multivariate analysis failed to demonstrate any possible risk factor for post operative complications, including Gender (-1.53 to 2.81 95% CI, p=0.52), Age (-0.34 to 1.15 95% CI, p=0.25), BMI (-0.041 to 0.019 95% CI, p=0.43), ASA score (-0.15 to 0.54 95% CI, p=0.24) or medications (-0.25 to 0.28 95% CI, p=0.88). In addition, out of various operative factors, including operation Urgency, Surgical Approach and surgery duration, only the latter was found to be correlated with post operative complications (0.013 to 0.035 95% CI, p< 0.001).

Conclusion: Patients suffering from inflammatory bowel disease undergoing abdominal wall hernia surgery are prone to more post operative complications. Larger scale studies are needed to assess possible risk factors.

Disclosure: Nothing to disclose

P1433 WITHDRAWN

P1434

COMBINED ENDOSCOPIC VACUUM THERAPY WITH A PROGRAMMED RINSING AND CLEANSING SYSTEM FOR ENDOSCOPIC CLOSURE OF GASTROINTESTINAL PERFORATIONS, ANASTOMOTIC LEAKAGE AND ABSCESES

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Introduction: Endoscopic vacuum-therapy (eVAC) has been established for the therapy and closure of postoperative anastomotic leakage and chronic insufficiency with intraabdominal abscesses of the colorectum and esophagus. The use of a standardized eVAC system vacuum therapy with a sponge requires regular exchange of the sponge every 72 hours. Several exchanges are mandatory and a long lasting durable period is often necessary to achieve a final closure of the defect.

Aims & Methods: We developed a customized system for combined, intermittent rinsing and vacuum therapy for larger leakages and intraabdominal abscesses. We used a customized sponge (V.A.C. VERAFLOR CLEANSE™) with two integrated inner tubes, one for flushing and rinsing, the second tube for vacuum therapy. Further, we used a programmable vacuum pump system for negative pressure therapy combined with programmed intermittent rinsing and cleansing (V.A.C. VERAFLOR™) with a defined volume of special irrigation solution (Granudacyn).

Results: We report a case series of 4 patients with postsurgical defects in large abscesses of the lesser pelvis after anterior rectum resection (3 patients) and of the mediastinum after proximal esophageal resection. The abscesses were all large with several deep fistulas in the lesser pelvis with partly contact with intraperitoneal cavity and in the complete mediastinum, respectively. All patients received conventional eVAC therapy before without significant improvement (mean: 2.5 changes of the sponge).

We achieved very clean wound situations in a comparable very short period. In addition, the induction of granularity, closure of the abscess cavity and healing was induced very rapidly. Overall, only 1-3 sponge exchanges (mean: 1.75) of the system - after 72 hours each - was required for complete closure of the defects.

Conclusion: The programmed intermittent rinsing and irrigation combined with eVAC using a customized sponge and programmed sequence is significant improvement of the conventional vacuum system of eVAC therapy for endoscopic closure especially of large postsurgical defects. Direct comparisons with conventional eVAC systems are mandatory in prospective, comparable trials.

Disclosure: Nothing to disclose

P1435

PATIENTS WITH PRIOR HISTORY OF OPIOID ABUSE DISORDER WHO UNDERGO BARIATRIC SURGERY ARE AT A HIGHER RISK FOR POST-SURGICAL COMPLICATIONS AND MORBIDITY

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Introduction: Opiate abuse is a major public health issue in the US. Despite increased awareness opiates continue to be abused by many patients and its effects on healthcare outcomes are a priority to investigate. The impact of opiates use disorder (OUD) in elective bariatric surgery (BSx) and the immediate post-operative period are unknown. We aim to investigate outcomes of OUD patients undergoing BSx.

Aims & Methods: The 2016 and 2017 National Inpatient Sample (NIS) database was queried for all discharges with using ICD10-CM/PCS codes of BSx. We excluded those with underlying gastrointestinal malignancies including: gastric, pancreatic, esophageal, intestinal and hepatobiliary. Patients were divided between OUD patients and non-opioid abusers. Primary outcome was in-hospital mortality. Secondary outcomes were in-hospital complications such as: shock, systemic inflammatory response syndrome (SIRS), sepsis, mechanical ventilation, parenteral nutrition, acute kidney injury (AKI), requirement of blood products and post-procedural complications such as: vomiting, bleeding, ileus, intestinal obstruction, mesenteric thrombosis, length of stay (LOS), total healthcare utilization charges. Multivariate regression analysis was performed to adjust for potential confounders.

Results: A total of 425,029 of BSx procedures were identified out of which 0.4% (n=1,659) had a concomitant diagnosis of OUD. Patients with OUD were more likely to be male (65.4% vs 75.8%; $P < 0.01$), older (50.2 vs 47.1 years; $P < 0.01$), white (70.8% vs 61.4%; $P < 0.01$), to have a Charlson index ≥ 3 (23.5% vs 22.0%; $P < 0.01$), to have Medicare as primary payer (35.2% vs 18.9%; $P < 0.01$), to be admitted in the Western region of the US (32.8% vs 18.7%; $P < 0.01$). OUD patients were more likely to have concomitant tobacco use disorder (1.8% vs 0.4%; $P < 0.01$), alcohol use disorder (7.8% vs 0.8%; $P < 0.01$), cannabis use disorder (3.3% vs 0.3%; $P < 0.01$), and to have type 1 diabetes (1.2% vs 0.4%; $P < 0.01$). On multivariate analysis, there was not a significant difference in mortality, however on secondary endpoints, OUD patients had higher risk for endotracheal intubation (aOR 3.48; $p < 0.01$), prolonged mechanical ventilation (aOR 2.51; $p < 0.01$), SIRS (aOR 5.60; $p < 0.01$), sepsis (aOR 4.57; $p < 0.01$), AKI (aOR 2.37; $p < 0.01$), higher rate of post-procedural complications including: post-surgical bleeding (aOR 2.12; $p = 0.04$) requirement of blood transfusion (aOR 3.93; $p < 0.01$), intestinal obstruction (aOR 3.55; $p < 0.01$), and composite all-cause complications (aOR 3.36; $p < 0.01$). OUD patients had longer hospital LOS (4.01 days; $p < 0.01$) and higher total hospitalization charges (38,306.03US\$; $p < 0.01$).

Conclusion: Patients with prior history of OUD who undergo BSx are at a higher risk for post-surgical complications and morbidity, and significantly impacts our healthcare system. Efforts to mitigate substance abuse, including OUD in BSx candidates has the potential to decrease post-surgical complications, morbidity, and can improve the burden on our health-care system.

Disclosure: Nothing to disclose

P1436

TUNNELED PERITONEAL DRAINAGE CATHETER PLACEMENT FOR REFRACTORY MALIGNANT ASCITES: SINGLE-CENTER EXPERIENCE IN 92 PATIENTS

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Introduction: Advanced cancer patients with refractory ascites do not often respond to dietary sodium restriction and diuretics. If left untreated, increasing ascites may contribute to the development of hyponatremia, hepatorenal syndrome, umbilical herniation, and spontaneous bacterial peritonitis and has a significant impact on the patient's quality of life. To avoid repeated paracentesis and multiple hospitalizations, a permanently inserted catheter in the abdominal cavity can be considered. Patients can drain their ascites independently of health care staff or facilities, at home, at times that they need to control symptoms, and to a reasonable degree, so that many complications can be prevented.

All these factors contribute to better symptom control and QOL. Family caregivers benefit as well. There are some risks associated with permanent catheter usage that should be addressed. The most important is infection, and others are fluid leakage, drain obstruction, dislodgment and cellulitis.

Aims & Methods: To determine the safety and effectiveness of tunneled peritoneal catheters in the management of refractory malignant ascites. Between January 2015 and April 2020, 92 patients with malignant ascites who required repeated LVP underwent tunneled peritoneal catheterization. We used The ASEPT® Peritoneal Drainage System. Using the Seldinger technique. All catheter placements were performed under local anesthesia according to manufacturer's instructions. Briefly, the peritoneal cavity was accessed with a 19-gauge coaxial needle using ultrasound guidance and a guidewire was advanced into the peritoneal cavity. A subcutaneous tunnel was prepared in the mid-abdomen. The peritoneal site was sequentially dilated, and a peelaway sheath was introduced over the guidewire into the peritoneal cavity. The catheter drainage system was advanced into the peel-away introducer sheath and positioned in the dependent aspect of the abdomen or pelvis. Ultrasound imaging was used to confirm good position within the abdomen. The dermatotomy site was closed with suture. Technical success was defined as the insertion of the catheter in a satisfactory intraperitoneal position with initial drainage of ascites. Immediate and late complications were recorded. The follow-up was performed with frequent phone contacts or day-hospital admission in case of problems. All patients completed a quality of life survey.

Results: A total of 92 patients (40 M/ 52F, mean age 64 years) underwent tunneled peritoneal catheter placement for refractory malignant ascites in our GI department. Technical success was 100% with no immediate complications. 19 patients (20,65 %) experienced minor and major complications. Nine patients developed a catheter-associated infection. The remaining complications included leakage at the dermatotomy site (N = 4), catheter dislodgement (N = 2), obstruction (N = 2), and cellulitis of the tunnel tract (N = 2). Patients who developed a catheter-associated infection had a significantly longer catheter dwell time compared to those who did not develop an infection.

Conclusion: Tunneled indwelling peritoneal catheters provide a relatively safe and cost-effective alternative to serial LVP in most patients with malignant ascites. Complication rate was acceptable and balanced by the benefits of the technique which avoided frequent LVP and associated complications. However, clinicians should be aware of an increased risk of peritonitis in long-term use.

Disclosure: Nothing to disclose

P1437

MICROPERFORATION DURING ENDOSCOPIC SUBMUCOSAL
DISSECTION: TO TREAT OR NOT TO TREAT?Morão B.¹, Ferreira A.O.², Lopes Cravo M.³¹Hospital Beatriz Angelo, Lisbon, Portugal, ²Hospital Beatriz Angelo, Gastroenterology Department, Lisbon, Portugal, ³Hospital Baetriz Angelo, Surgery Department, Lisbon, Portugal**Contact E-Mail Address:** barbara.tsmorao@gmail.com**Introduction:** Perforation during endoscopic submucosal dissection (ESD) can be managed with clips. However, the treatment of microperforations (areas of visible muscle damage with vessels exposure) is not well established. Clipping in these areas does not always prevent gastrointestinal bleeding (GIB), which could be explained by flow distribution phenomena with increased pressure and subsequent higher risk of bleeding from adjacent vessels.**Aims & Methods:** Our goal was to access if clipping in areas of microperforation increases the incidence of post-ESD bleeding. We conducted a retrospective single-center cohort study including patients with lesions removed by ESD from January 2018 to August 2019. Primary outcome was defined as the incidence of clinically significant GIB (hemoglobin drop >2g/dL or need for endoscopic hemostasis) within 15 days after the procedure. A multivariate analysis adjusted for confounding factors was performed.**Results:** Forty-five patients were included, 73% of whom were men with mean age of 71±8 years. Anti-thrombotic medication was taken in 17/45 patients and 3/45 and 2/45 had history of chronic kidney disease and cirrhosis, respectively. Mean lesion size was 29±19mm diameter and they were located in the stomach (23/45), esophagus (1/45), colon (4/45) or rectum (17/45). The mean duration of the procedures was 131±92 minutes. Visible vessel hemostasis was performed in 38/45 patients, and 8/45 required the use of coagrasper. Perforation occurred in 3/45 patients (managed with clips). Microperforation and subsequent clipping occurred in 24/45 patients. GIB was seen in 7/45 patients, with a median time of 24 hours after the procedure. The incidence was higher (71% vs. 29%) in patients with microperforation and clip application (OR 2.5, IC95% 0.43-14.5, p=0.31). There was no change in bleeding risk when adjusting for lesion size (OR 3.67, IC95% 0.58-22.77, p=0.17), specimen size (OR 6.38, IC95% 0.80-51.1, p=0.08) or antithrombotic use (OR 2.19, IC95% 0.37-13.15, p=0.39).**Conclusion:** In this cohort, clipping in areas of microperforation did not result in higher risk of GIB (p=0.31). This could be a safe approach to reduce the risk of post-ESD bleeding, and prospective studies should try to demonstrate its effectiveness.**Disclosure:** Nothing to disclose

Poster presentations COVID-19

Poster Presentations COVID-19

COVID-19

09:00-19:00 / Poster Exhibition

P1438

REDUCING THE RISK FOR ENDOSCOPIST WITH A BOX

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Introduction: Upper GI endoscopy is an aerosol generating procedure, and therefore, amid of pandemia, carries a risk for operators to be infected with SARS COV2. Personal protective equipment (PPE) are able to reduce the risk of virus dissemination. We considered the possibility to increase the protection for the operators with a transparent box over the patient's head, adapting to endoscopy a model published elsewhere (1).

Aims & Methods: We have modified the Canelli's aerosol box in order to adapt to endoscopy.

The box consisted of four plexiglas transparent walls to be put on the head of the patient, with two holes for the hands of the nurse and a door for the scope. The box was manufactured by an acrylic factory (Plexismart, Guidonia, Italy) and donated to our hospital. We evaluated the safety and the ease of use of this box in a series of 30 consecutive upper GI endoscopies in patients affected of or suspected for SARS COV 2 infection.

Results: In 30 gastroscopies, box did not disturbed both the gastroenterologist's or the nurse's activity. There have been no need to remove it during the procedures. An average of additional 2 minutes time was needed for placing and removing the box.

Conclusion: In conclusion, the "aerosol box" is a cheap and easy to use device that could help to reduce the risk of infection by aerosol carried pathogens.

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Disclosure: Nothing to disclose

P1439

DIFFERENTIAL EFFECTS OF COVID-19 PANDEMIC AND LOCKDOWN IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS) AND IN NON-IBS SUBJECTS

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Introduction: While all resources have been mobilized to fight COVID-19, other diseases have been left behind with risks of worsening. Recently, alerts have been given on the psychological risks of confinement during the pandemic in patients with chronic disease and in healthy subjects, with the possibility of developing post-traumatic stress.

Aims & Methods: This study aimed to analyze the consequences of lockdown and pandemic stress in participants with and without Irritable Bowel Syndrome (IBS).

An online survey was proposed to people with IBS (members of the French patients' association) or without IBS, 15 days after the start of confinement in France, during the exponential phase of the pandemic. The questionnaire included questions about socio-demographic data, conditions of confinement, activities carried out, IBS characteristics, measurement of stress level, consequences on sleep, fatigue, anxiety and depression, and quality of life (both perceived non-specific and specific for IBS).

Results: From March 31 to April 15, 2020, 304 participants (232 with IBS and 72 without) were included in the survey. Age, level of education, financial resources, living space per person and activities performed during confinement were identical in both groups. Stress linked to fear of COVID-19, lockdown and financial worries was at the same level in both groups, but the psychological consequences and deterioration of quality of life (QOL) were both higher in IBS participants. In a univariate analysis, working from home, solitary confinement, and low household resources had a variable impact on the scores of depression, anxiety, fatigue and non-specific QOL perceived, but in a multivariate analysis, the only factor explaining a deterioration of non-specific QOL was the fact of suffering from IBS.

Conclusion: Stress linked to the COVID-19 pandemic and confinement is high in both IBS and non-IBS participants, with higher psychological and QOL consequences in IBS patients than might be explained by an impairment in coping capacities.

Disclosure: Nothing to disclose

P1440

IMPACT OF THE SARS-COV-2 PANDEMIC ON GASTROENTEROLOGY UNITS IN ITALY: A NATIONAL SURVEY

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Introduction: In Italy, the spread of the SARS-CoV-2 pandemic has stressed the entire healthcare system and required a huge re-organization of many divisions, including those of Gastroenterology. Many of them have been converted to COVID Units to deal with the emergency, while others were forced to reduce the routine workload to prevent the infection spreading, with consequent impairment of the health services provided and potential consequences for patients.

Aims & Methods: This is a prospective observational web-based survey aimed to assess the impact of SARS-CoV-2 pandemic on Gastroenterology Units in Italy. All members of the Italian Society of Gastroenterology (SIGE) were invited to answer a 39-point multiple-choice web-based survey.

Results: Data of 121 hospitals from all 20 Italian regions were analyzed. Overall, 10.7% of Gastroenterology divisions have been converted to COVID Units. Outpatients consultations, endoscopic and ultrasound procedures were limited to urgencies and oncology indications in 85.1%, 96.2% and 72.2% of Units, respectively, and 46.7% of Units suspended the screening for colorectal cancer. In order to guarantee the ordinary follow-up of outpatients, 83/121 (68.6%) divisions activated a remote consultancy service (63.9% by phone, 31.3% by email, 4.8% by video).

Overall, 112/121 (92.6%) GI Units issued and followed a specific protocol for the management of patients with suspected or confirmed SARS-CoV-2 infection. The 72.2% of the staff received proper training for the use of personal protective equipment, although 45.5% did not have sufficient devices for an adequate replacement. With regard to PPE availability, N95/FFP2-3 masks were available in 91/121 (75.2%), surgical masks in 115/121 (95.0%), gloves in 117/121 (96.7%), disposable gown in 100/121 (82.6%), hairnet in 104/121 (85.9%), goggles in 78/121 (64.5%) and boots in 57/121 (47.1%) of divisions.

Finally, in 41/121 GI divisions (33.9%) there was at least one healthcare professional who got infected, in a total of 132 subjects, of which 121/132 from divisions not-converted to COVID Units and 75/132 from high-prevalence areas. In 56/121 (46.3%) hospitals, the exposed personnel undergo a nasopharyngeal swab to ruleout infection only if symptomatic.

Conclusion: This is the first study to evaluate, at a country level, the impact of SARS-CoV-2 outbreak on Gastroenterology divisions. Substantial changes of practice and reduction of procedures have been recorded in the entire country. The long-term impact of such modifications is difficult to estimate but potentially very risky for many digestive diseases.

Disclosure: Nothing to disclose

P1441

A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE COVID-19 ASSOCIATED LIVER INJURY

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Introduction: The novel coronavirus disease 2019 (COVID-19) has affected more than 3 million people globally. Data on the prevalence and degree of COVID-19 associated liver injury among patients with COVID-19 remain is limited.

Aims & Methods: We conducted a systematic review and meta-analysis to assess the prevalence and degree of liver injury between patients with severe and non-severe COVID-19. We performed a systematic search of three electronic databases (PubMed/MEDLINE, EMBASE and Cochrane Library), from inception to 24th April 2020. We included all adult human studies (>20 subjects) regardless of language, region or publication date or status. We assessed the pooled odds ratio (OR), mean difference (MD) and 95% confidence interval (95%CI) using the random-effects model. The cut-off for abnormal liver enzymes were as the following: ALT, AST or GGT>40U/L, total bilirubin>17mmol/L and albumin<40g/L. Severe COVID-19 was defined based on the pre-defined criteria in respective studies.

Results: Among 1543 citations, there were 24 studies (5961 subjects) which fulfilled our inclusion criteria. The pooled odds ratio for elevated ALT (OR=2.8, 95%CI: 1.8-4.3, I²=63%), AST (OR=3.4, 95%CI: 2.3-5.1, I²=59%), hyperbilirubinemia (OR=1.9, 95%CI: 1.1-3.1, I²=30%) and hypoalbuminemia (OR=8.8, 95%CI: 4.1-19.0, I²=46%) were higher subjects in severe disease. Compared to survivor, ALT elevation is more common among COVID-19 non-survivor (OR=2.3, 95%CI=1.2-3.7, I²=44%). Studies with high Lopinavir/ritonavir usage had higher pooled risk of AST elevation (OR=3.3, 95%CI=1.6-6.8, I²=53%) when compared to studies with low Lopinavir/ritonavir usage. When proportion of subjects with baseline chronic liver disease and ICU admission were considered, the risk of COVID-19 associated liver injury remained higher in those with severe disease. Severe COVID-19 patients have higher risk of GGT elevation after adjusting to Lopinavir/ritonavir usage. This finding suggests a direct cytopathic link between SARS-COV-2 and the infected ACE-2 positive cholangiocytes during COVID-19.

Conclusion: Although COVID-19 associated liver injury is more common in severe COVID-19, it is generally mild. Our finding suggest Lopinavir/ritonavir is potentially hepatotoxic. As severe COVID-19 and drug-induced liver injury are more common in elderly, we recommend monitoring of liver function when Lopinavir/ritonavir is used in subjects with severe COVID-19.

Disclosure: Nothing to disclose

P1442

CLINICAL CHARACTERISTICS AND PROGNOSIS OF COVID-19 IN A SPANISH COHORT OF INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: COVID-19 has rapidly become a health emergency throughout the world, resulting in > 2.6 million of people infected. A high proportion of patients with inflammatory bowel disease (IBD) are on immunosuppressive therapies which are associated with an increased risk of infections. In this regard, the clinical course of COVID-19 in patients with IBD and the potential risk due to immunosuppressive treatments is still unknown.

Aims & Methods: The aim of this study is to describe characteristics and prognosis of COVID-19 in a cohort of IBD patients. We conducted an observational study in IBD patients with suspicion of COVID-19. We considered high-risk patients those under immunosuppressive treatments (i.e. immunomodulators, biologics and/or corticosteroids), and low-risk patients those without comorbidities and not receiving the aforementioned treatments. Following recommendations by the Health Ministry, we performed real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) of nasopharyngeal swab and chest X-ray on all high-risk patients. World Health Organization definitions for confirmed, probable and suspected cases were used. Baseline and IBD-related features were collected.

Results: 50 cases of COVID-19 in IBD patients have been registered in our institution up to date. 62% were receiving immunomodulators or biologics. 32.6% (16 patients) had visible pneumonia on chest X-ray, of which 50% were high-risk and low-risk patients respectively. 12 patients (24%) required hospital admission, with a mean hospital stay of 8.5 days (SD 6.6). Low-risk patients had to be admitted more frequently than high-risk patients (42% vs 13%, $p=0.01$). Mean age (59.79 vs 41.7, $p=0.0001$) and concomitant high blood pressure (36% vs 12%, $p=0.04$) were higher among patients at low-risk. Anti-TNFs were associated with a lower risk of hospital admission (0% vs 35%, $p=0.006$) and pneumonia (OR 0.5, $p=0.489$).

Conclusion: Our cohort of IBD immunosuppressed patients presented a low need for hospital or intensive care unit admission. Mortality was similar to that of the general population. Anti-TNFs were associated with a lower risk of pneumonia and hospital admission.

Disclosure: MSA has served as speaker for Janssen and has received financial support for travelling and educational activities from Takeda, Janssen, Tillots and Ferring. CSF has received financial support for travelling and educational activities or has received fees as a speaker or consultant from Ferring, MSD, Janssen, Takeda and Tillots pharma. EMA has received financial support for travelling and educational activities or has received fees as a speaker or consultant from Ferring, MSD, AbbVie and Takeda. JLRG has received financial support for travelling and educational activities from Janssen, Takeda, Ferring, Tillots pharma, Faes pharma, Norgine and Casen. JPC has received financial support for travelling and educational activities from Abbvie, Janssen, Kern Pharma, Pfizer, MSD, Amgen, Takeda, Ferring, Shire, Tillots pharma. JNB has received financial support for travelling and educational activities from Abbvie, Janssen, Pfizer, Takeda. MDMA has received fees as a speaker, consultant and advisory member for o has received research funding from MSD, AbbVie, Hospira, Pfizer, Takeda, Janssen, Shire Pharmaceuticals, Tillots Pharma, Faes Pharma. Remaining the authors do not disclose conflicts of interest.

P1443

COVID-19 PATIENTS BENEFIT FROM ORAL BACTERIOTHERAPY

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Introduction: The cells of the intestinal mucosa could be a reservoir for coronaviruses¹. In the acute phase, only 10% of COVID-19 patients present virus cDNA in the blood, but almost 50% of them excrete it in the stools. The infectious form of the virus was even identified several times, suggesting that the orofecal route is a mode of contamination¹. The gut involvement might explain the wide variation in viral load from one test to another in the same person as if the virus were hiding there². Chinese researchers have investigated changes in the microbiota in the patients who have died for COVID-19 infection. The sequencing of their microbiota revealed a significant decrease in *bifidobacteria* and *lactobacilli*, the main families of symbiotic bacteria, as well as an increase in opportunistic bacteria such as *Corynebacterium* or *Ruthenibacterium*¹. Intestinal dysbiosis has a long-reaching immune impact on the pulmonary immune system³, and hence might be an additional risk for respiratory distress induced by COVID-19. In this context, the use of oral bacteriotherapy might be a therapeutic option.

Aims & Methods: This study aimed to evidence, for the first time, the effectiveness of a specific oral bacteriotherapy in treating COVID-19. We provide a report of 70 patients positive for COVID-19, hospitalized between March 9th and April 4th, 2020. All the patients had fever, required non-invasive oxygen therapy and presented a CT lung involvement on imaging more than 50%. Forty-two patients received, for seven days, hydroxychloroquine, antibiotics, and Tocilizumab, alone or in combination.

A second group of 28 subjects also received oral bacteriotherapy using the specialized formulation of eight bacterial strains contained in the product Sivomixx® (Ormendes SA, Lausanne, Switzerland). The oral bacteriotherapy involved the use of 2,400 billion bacteria per day administered in two equal doses separated by a 12h time interval.

Results: The two cohorts of patients were comparable for age, sex, laboratory values, concomitant pathologies, and the modality of oxygen support. Within seventy-two hours, nearly all patients treated with bacteriotherapy showed remission of diarrhea and other symptoms as compared to less than half of the not supplemented group. The estimated risk of developing respiratory failure was eight-fold lower in patients receiving oral bacteriotherapy. Both the prevalence of patients transferred to ICU and mortality were higher among the patients not treated with oral bacteriotherapy.

Conclusion: A specific bacterial formulation showed a significant ameliorating impact on the clinical conditions of patients positive for SARS-CoV-2 infection. These results also stress the importance of the gut-lung axis in controlling the COVID-19 disease.

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al. Immunodepletion with Hypoxemia: A Potential High-Risk Subtype of Coronavirus Disease. *MedRxiv* 2019; 2020.03.03.20030650. 3. Chiu L, Bazin T, Truchetet ME, et al. Protective microbiota: from localized to long-reaching co-immunity. *Front. Immunol.* 2017; 8: 1678.

Disclosure: Nothing to disclose

P1444 WITHDRAWN

P1445

EFFICACY OF ENDOSCOPIC TRIAGE DURING THE COVID-19 OUTBREAK AND INFECTIVE RISK

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Introduction: A SARS-CoV-2 outbreak has spread worldwide, Italy being a high-incidence country. As a consequence of the new circumstances, almost all endoscopic units underwent in-depth re-organization involving logistics, scheduling and selection of patients. No data has been available about the efficacy of the novel *endoscopic triage* adopted to limit the access to the endoscopic procedures (1).

We analyzed the efficacy of this newly adopted triage compared to that used during the non-Covid-19 era.

Aims & Methods: From the 9th to the 27th March 2020, in the Endoscopy Unit of the Fondazione IRCCS Ca' Granda, a tertiary referral Center in Milano, a new selection of patients undergoing endoscopic procedures has been started, to reduce the number of investigations and consequently the viral spread and contagions.

Clinical, demographic data of the patients have been recorded. Indications, type of endoscopy, endoscopic findings (subtyped in major and minor findings), finding rate (major and minor findings, FR) and diagnostic yields (major findings, DY) as previously defined in literature (2,3) have been analysed and compared to the endoscopic procedures performed in the corresponding March 2019 timeframe.

All patients were called at least 21 days after the endoscopy in order to evaluate the possibility of a Covid-19.

Results: Accordingly to the novel triage, the number of endoscopic procedures performed during Covid-19 outbreak drastically dropped from 530 to 91 (-84%).

Globally, the FR and DY were 83%(74-89) vs 71%(66-73) (p 0.015) and 56%(46-65) vs 43%(38-47) (p 0.03) on March 2020 and March 2019, respectively. Age and sex were not associated with DY neither on 2020 nor 2019. In **Table 1** the DY of the routinely endoscopic procedures are reported in detail.

In terms of operative EGDS and CLS, in 2020 there was a significant increase of operative endoscopies, which represented the 34% of the total endoscopies in March 2020 vs. 22% in March 2019 (p=0.02).

All the patients were recalled and neither cases of onset of Covid-19 like symptoms nor positive nasopharyngeal swabs PCR have been evidenced among the patients and also their cohabitants.

Conclusion: The present study is the first evaluating endoscopic performance while adopting a new patients' triage compatible with the actual pandemic scenario. Following the novel criteria, the number of procedures has drastically dropped (-84%) with a significant increase of FR and DY. Similarly, the percentage of operative endoscopies has been significantly higher. No Covid-19 onset or infection have been noted after endoscopic procedures in respect of the incubation period.

Concerning the follow-up, it is also clear that re-programming cancelled endoscopies should be carried out carefully and by means of telemedicine.

Type of endoscopy	March 2020	March 2019	P value
EGDS (%)			
FR (%)	90 (76-96)	70 (64-75)	0.0001
DY (%)	45 (64-89)	79 (39-51)	0.0001
Colonoscopy (%)			
FR (%)	83 (69-92)	69 (63-75)	0.09
DY (%)	33 (20-48)	30 (25-37)	0.71

[Table 1: Finding rate and diagnostic yield of EGDS and CLS in 2020 and 2019]

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P1446

RISK OF COVID-19 IN CELIAC DISEASE PATIENTS

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Introduction: Celiac disease (CeD) is an autoimmune multiorgan disease affecting the small bowel in genetically predisposed subjects, precipitated by the ingestion of gluten. CeD has been associated with a higher risk of infections in several papers, including influenza and community-acquired pneumonia. The severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) responsible for Coronavirus disease 2019 (COVID-19) has been declared a pandemic in March 2020. Several regions in Northern Italy, including the Veneto region, went into emergency lockdown on the 8th of March and the Government extended the lockdown to the whole Country three days later.

Aims & Methods: In keeping with the above considerations, the aim of our study was to investigate whether adult patients with CeD have an increased risk of COVID-19 infection. Between the 9th and the 11th of April, we contacted all CeD patients regularly followed-up at the University Hospital of Padua (Veneto, Italy) and included in our CeD registry (approved by the research ethics committee of the Azienda Ospedaliera di Padova under the protocol 4680/AO/19) and on a gluten free diet from at least six months. Patients were asked if they have been infected with COVID-19; if they have been in contact with someone (friends or family components) infected by

COVID-19; if they were experiencing flu-like symptoms suspected for COVID-19 infection and finally if they had undergone naso-pharyngeal swabs for SARS-CoV-2.

Results: Among the 171 patients included in our registry and on gluten free diet from at least six months, we contacted 138 CeD subjects (80.7%), aged 45.2 years old, 73.9% were females on a gluten-free diet from a mean of 6.6 years (SD 6.0). Two patients had a diagnosis of refractory celiac disease type one and one of refractory celiac disease type 2. Among them, none reported to have been diagnosed with COVID-19, whereas 19 CeD patients experienced flu-like symptoms with 1 of them having undergone a negative naso-pharyngeal swab.

Further, 11 patients reported a member of their family or close contact with respiratory symptoms suggestive of COVID-19 infection, with 2 of them undergoing naso-pharyngeal swab with negative results. Meanwhile, on the 11th of April at Padua University Hospital we had 97 COVID cases hospitalised in non-intensive care units and 20 in intensive care units because of severe COVID-19 infection.

Conclusion: Our data show the absolute absence of COVID-19 diagnosis in our population, although 18 subjects experienced flu-like symptoms with only one having undergone naso-pharyngeal swab. As a consequence, we cannot exclude in this subgroup the presence of undiagnosed infections. On the other hand, the lack of patients with severe flu-like symptoms requiring hospitalisation or at least COVID-19 assessment further support the absence of risk for COVID-19 infection in patients with CeD.

The main limitations of this study are related to the observational nature and the short length of follow-up. However, according to our routine clinical practice, patients can communicate any complication to our team through a dedicated e-mail and no signs of SARS-CoV-2 infection or severe respiratory symptoms have been communicated at the time of writing (May 11th, 2020). We only evaluated patients on a gluten free diet, so far no data on the risk at the time of diagnosis can be extrapolated from this study.

Disclosure: Nothing to disclose

P1447

PREVALENCE AND CHARACTERISTICS OF GASTROINTESTINAL SYMPTOMS IN A LARGE WESTERN COHORT OF PATIENTS WITH CORONAVIRUS DISEASE 2019: A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: There is increasing evidence to support a gastrointestinal involvement of Covid-19, and gastrointestinal symptoms are reported to be common in this population. However, most data are retrospective and come from Eastern countries.

Aims & Methods: Our aim was to describe the prevalence and the characteristics of gastrointestinal symptoms in a large Italian cohort of patients with Covid-19.

In this single-centre, prospective observational cohort study, we assessed gastrointestinal symptoms in all hospitalized patients with Covid-19 at our hospital, through the Gastrointestinal Symptoms Rating Scale (GSRS), both at diagnosis and after therapy. Univariate and multivariate analysis for critical clinical picture and death were obtained.

Results: In the study period, we enrolled 420 patients with COVID-19 infection (M= 238, F= 182, median age 61 year old). Of them, 247 (59%) reported at least one gastrointestinal symptom at the GSRS. Overall, most common symptoms were diarrhoea (37%), nausea (19%), urgency (17%), loose stools (16%). At the GSRS evaluation, the highest mean scores were attributed to urgency (mean= 4), diarrhoea (mean=3.8), nausea (mean=3.6), loose stools (mean=3.4). In 117 patients (47%), symptoms occurred after infection, while in 130 patients (53%) they appeared after the start of COVID-19 therapy.

A cluster of upper gastrointestinal symptoms was significantly more frequent in patients who became symptomatic after infection, including heartburn (15/117 vs 4/130, p=0.007), acid reflux (15/117 vs 6/130, p=0.02), hunger pains (10/117 vs 1/130, p=0.003), nausea (43/117 vs 35/130, p=0.04), and rumbling (11/117 vs 3/130, p= 0.02), while diarrhoea was significantly more common in patients who developed symptoms after therapy (57/117 vs 98/130, p<0.0001). Gastrointestinal symptoms (OR 2.35, 95% IC 1.04 to 5.3, p= 0.04) were found to be independent predictors of critical clinical picture and transfer to ICU.

Conclusion: This is the first prospective study, and the largest Western cohort, to describe the clinical characteristics of gastrointestinal symptoms in patients with Covid-19 so far. Through a validated scoring system, we found that a considerable rate of patients with Covid-19 presents with gastrointestinal symptoms, but that in nearly a half of cases they appear after Covid-19 related therapy, with different patterns of symptoms between the two groups.

Finally, we found also that gastrointestinal symptoms could predict a worse clinical picture. Our results may be useful to disentangle characteristics and relevance of the gastrointestinal involvement in patients with Covid-19.

Disclosure: Nothing to disclose

P1448

EFFECTS OF COVID-19 PANDEMIC ON HOSPITALIZATION FOR UPPER GASTROINTESTINAL BLEEDING IN HONG KONG: A POPULATION-BASED STUDY

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Introduction: The COVID-19 pandemic has resulted in major disruption to delivery of healthcare services globally, including emergency medical services.

Aims & Methods: To determine the effects of COVID-19 pandemic on the hospitalization rates for upper gastrointestinal bleeding (UGIB) and patient's outcome in Hong Kong. The first local case of COVID-19 was reported on 23 January 2020 in Hong Kong. We retrieved all hospitalization records for UGIB between October 2016 to March 2020 in Hong Kong from the territory-wide electronic health database. Time trend analysis was performed for hospitalization rates for UGIB during this period. Autoregressive Integrated Moving Average model (ARIMA) was constructed to predict the numbers of patients with UGIB, rebleeding rates, GIB related mortality, causes of UGIB, rates of blood transfusion and endoscopic hemostasis, and overall length of hospital stay (LOS), to compare with the actual observed data after the first reported local case.

Results: There were a total of 8,105 hospitalizations related to UGIB (7,756 before and 349 patients after first local COVID-19 case). The observed numbers of UGIB per week was significantly lower after the COVID-19 outbreak (mean 35.4 vs 30.9, p < 0.01). In particular, the observed number of peptic ulcer and Mallory Weiss tear per week was significantly lower than pre-

dicted (mean 26.4 vs 20.3, $p=0.02$; 4.8 vs 3.3, $p=0.05$). Both the observed endoscopic hemostasis rate and blood transfusion rate of patients who presented with peptic ulcer bleeding showed a non-significant increase when compared to predicted values (77.1% vs 75.1%, $p=0.39$; 60.3% vs 51.3, $p=0.18$). The actual LOS was however shorter than the predicted LOS (9.1 vs 10.7, $p=0.03$).

However, there were no significant difference in rebleeding rates at day 7 (7.2% vs 7.1%, $p=0.96$) and UGIB related mortality (0.7% vs 0.8%, $p=0.76$) after the COVID-19 outbreak (Table 1).

	Predicted	Actual	P value
Mean number of cases per week	35.4	30.9	<0.01
Rebleeding rate with 7 days	7.2%	7.1%	0.96
UGIB-related mortality	0.7%	0.8%	0.76
Length of stay (days)	10.7	9.1	0.03
Main cause of UGIB (Mean number of cases per week)			
Peptic ulcer bleeding	26.4	20.3	0.02
Variceal bleeding	2.2	2.2	0.97
Hemorrhagic gastritis	2.3	1.8	0.21
Hemorrhagic duodenitis	0.2	0.2	0.96
Esophageal hemorrhage	0.3	0.3	0.74
Mallory Weiss tear	4.8	3.3	0.05
Angiodysplasia	0.5	0.3	0.29
Dieulafoy lesion	0.5	0.7	0.70
Other causes	0.2	0.1	0.10

[Comparison of UGIB characteristics after the local COVID-19 outbreak]

Conclusion: Since the COVID-19 outbreak in Hong Kong, there was a significant reduction in the number of patients presented to hospital with UGIB, particularly those with less severe bleeding. Although the outcome of patients who were not admitted to hospital cannot be determined, there was no significant changes in other measurable outcomes in UGIB patients who were hospitalized during the COVID-19 pandemic.

Disclosure: Nothing to disclose

P1449

CYTOSPONGE AS A TRIAGING TOOL TO UPPER GI ENDOSCOPY DURING COVID-19 PANDEMIC

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Introduction: In the COVID-19 pandemic, endoscopy services have been severely curtailed. Upper GI endoscopy poses particular concern due to aerosol generation throughout the procedure when clinical staff are by necessity in close proximity. This reduction in endoscopy provision means that some patients with Barrett's-related high-risk lesions and oesophageal cancer will have a delay in diagnosis, which may adversely affect outcomes. The Cytosponge is an oesophageal cell sampling device which can be administered by a single health-care professional in the office setting and aerosol is only generated in the last few seconds of the procedure during removal of the device. The cells retrieved can be assessed for cytological and immuno-histochemical abnormalities.

Aims & Methods: We performed a pilot study to investigate the feasibility and utility of a Cytosponge triage clinic to inform the necessity and urgency for further investigations in patients referred for rapid assessment of oesophageal symptoms.

Patients referred for urgent endoscopy with mild/moderate dysphagia or other severe oesophageal symptoms who could swallow a capsule were invited to attend for a Cytosponge examination. The test was administered by a specialist nurse using personal protective equipment (PPE) for device withdrawal.

The retrieved cells were evaluated for atypia, the intestinal metaplasia biomarker TFF3 and for aberrant p53 expression. The sample was evaluated by an expert upper GI cytopathologist. The results were used to triage patients for further investigation.

Results: Between 8th and 30th of April 2020, 88 patients referred for urgent endoscopy were screened by telephone of which: 9 received fast-track endoscopy; 61 were reassured and offered advice and/or medication due to very mild symptoms; and 18 were deemed eligible for Cytosponge. 11 of the 18 eligible patients accepted the invitation and attended a Cytosponge clinic - 8 men and 3 women with an average age of 66 years (range 54-80).

The majority of the patients were referred with dysphagia, with a median Mellow score of 1 (range 1-3) and two patients were referred with severe chest pain upon eating. In three cases incomplete passage of the Cytosponge was suspected indicative of a possible obstructing oesophageal lesion. Two of these had atypical glandular cells with aberrant p53 expression suggestive of a cancer diagnosis, and the third had no gastric glandular cells on the sample confirming a likely obstruction. All three of these cases had suspected cancer confirmed by endoscopy and CT. Two cases had TFF-3 positive intestinal metaplasia on the Cytosponge suggestive of Barrett's oesophagus with no associated atypia and they have been recommended to have an endoscopy when services resume. The remaining patients had no abnormality detected and have been managed with telephone reassurance and medication as required.

Conclusion: Cytosponge is a feasible and useful diagnostic test in the COVID-19 pandemic. It allows for triage of patients referred with dysphagia and other oesophageal symptoms in order to minimise coronavirus infection risk while still providing prompt investigation and referral for suspected cancer.

Funding: Was provided by the COVID-19 fund to Cambridge University Hospitals NHS Trust and an MRC core grant to the Fitzgerald laboratory.

Disclosure: Rebecca Fitzgerald and Maria O'Donovan are named on patents for Cytosponge and related assays that have been licensed by the Medical Research Council to Covidien GI Solutions (now Medtronic). They are share-holders in Cyted Ltd which aims to provide solutions for early diagnosis. Other authors have no COI to declare.

P1450

IMPACT OF SARS-COV-2 PANDEMIC ON IBD PATIENTS IN OUR TERTIARY CENTRE - CROSS SECTIONAL STUDY

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Introduction: At the outbreak of an ongoing SARS-CoV-2 pandemic little was known about its impact on highly immunosuppressed IBD patients. Our IBD unit went under vigorous organisational changes in accordance with government "lock down" plan. Primary goals were maintenance of our accessibility and provision of all relevant information to our IBD pa-

tients. Consequences of coronavirus pandemic on emotional and psychological health are tremendous and earthquake that hit our area in the middle of the crisis certainly contributed to it.

Aims & Methods: After introduction of novel methods of patient regular monitoring (remote check-ups by scheduled phone calls and online consultancy, additional email addresses and telephone lines, adequate protective measures in infusion unit, online and printed informative brochures) we have invited our patients to complete anonymous questionnaire in order to reveal there's concerns and burden of emotional stress as well as satisfaction with provided healthcare.

Results: 103 adult patients (63.5% female, 59 had Crohn's disease, 39 ulcerative colitis and 5 IBD unclassified) fulfilled online questionnaire from April 1st to April 30th. 63.5% of participants were between 18 and 40-year-old and only 1.9% were older than 60, probably due to low computer literacy among elder population. 74 participants had disease duration >5 years and 54.4% were treated with biologics. Only 48.1% of our patient considered to be appropriately and on time informed about COVID-19 impact on there's health. 63.5% perceived themselves as high risk group of patients and vast majority considered social distancing and isolation as extremely important.

Moreover, half of participants refrained from interaction with household members even without being particularly advised to do so. 19 participants reported worsening of symptoms from the beginning of pandemic, although none of the patients discontinued recommended IBD therapy. Albeit 43.3% reported high emotional and psychosocial burden only 18.3% reported a need for psychological help. 13 of 91 lost their job or felt that they were under high risk of becoming unemployed. 66.3% were completely and 12.5% were partially satisfied with provided healthcare. 57.7% of participants considered virtual clinics as a convenient way of communication even after SARS-CoV-2 pandemic resolution. Until the end of April, we haven't recorded any COVID-19 positive IBD patient in our IBD clinic.

Conclusion: While the real psychological, socioeconomic and health consequences are yet to be assessed this pandemic helped to revealed important role of telemedicine. We believe that we have been able to establish effective and satisfactory communication channel during SARS-CoV-2 infection with younger subpopulation of our IBD patients. How much impact does this health crisis have on our elder subpopulation of IBD population is still unknown. Members of IBD team must put additional emphasis on communicating and helping to resolve high emotional and psychosocial burden that coronavirus pandemic have on IBD patients.

Disclosure: Nothing to disclose

P1451

MEDICAL CARE OF ATROPHIC GASTRITIS PATIENTS DURING COVID-19 PANDEMIC: RESULTS OF TELEMEDICINE IN A REFERRAL CENTER

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Introduction: Atrophic gastritis (AG) is a chronic condition, often affecting the elderly with one or more comorbidities, characterized by the absence or the presence of few specific symptoms, and the clinical interview is the mainstay of the face-to-face outpatient visits. At the end of February 2020 in Italy were reported the first cases of SARS-CoV-2 infection and since the beginning of March not-urgent outpatient visits were cancelled, so the vast majority of AG patients' visits were postponed. Telemedicine has

been used in some chronic diseases as a supportive care tool instead of face-to-face visits in order to properly establish the management of patients with chronic diseases during pandemic.

Aims & Methods: The aim of the study was to investigate the impact of SARS-CoV-2 pandemic on AG patients and to assess the presence of GI symptoms using telemedicine as tool of supportive care, in an academic hospital of a low risk region of central Italy. A cross-sectional study on AG patients who had a last face-to-face outpatient visit within the last two years was conducted. During telephone interviews, the personal risk perception for SARS-CoV-2 infection, the presence of symptoms related to infection (fever, cough, asthenia, anosmia/ageusia and diarrhea) and risk of infection exposure, were addressed. Furthermore, GI symptoms were investigated using a standardised questionnaire currently used in our department to investigate the presence, severity and frequency of new (onset during the SARS-CoV-2 pandemic) or already present (last face-to-face visit) GI symptoms and to establish the need of an urgent face-to-face outpatient visit or other medical intervention.

Results: Overall 218 pts were included and 151 (69.2%) responded to the telephone calls and adhered to the telemedicine interview. Female (F) were the 72.2% and median age was 67 years (range 30-89, 60.9% > 60yrs). Seventeen (11.3%, F 64.7%, median age 66yrs) referred at least one symptom suspect for SARS-CoV-2 infection (one of them, a man of 75 yrs, had radiological diagnosis of pneumonia with a favorable outcome), but only 1 patient was tested by nasopharyngeal swabs to rule out diagnosis of SARS-CoV-2 infection and resulted negative. Considering the risk of exposure, 19 (12.6%) pts had a job at risk for infection and 22 (14.6%) had a contact with hospitals or people working in a hospital. Risk perception for SARS-CoV-2 infection was none, low or high for 82 (54.3%), 38 (25.3%) and 31 (20.4%) respectively. Concerning GI symptoms, 17 (11.3%) presented new-onset symptoms, already treated by themselves or by the general practitioner, while 65 (43.0%) presented symptoms already present at the last visit. Dyspepsia (29.8%) was the most frequent upper GI tract symptom, whilst constipation (21.2%) for the lower GI tract. None of the pts presented red-flag symptoms requiring urgent outpatient face-to-face visit or medical intervention.

Conclusion: Despite the presence of symptoms suspicious for SARS-CoV-2 infection in about 10% of elder AG patients and one case of pneumonia, none of the interviewed patients had a negative outcome due to COVID-19. New GI symptoms occurred in a low proportion (11%) of patients, whose potential relationship to pandemic is unlikely as 80% of interviewed patients perceived a low or did not perceive any pandemic-related risk. Telemedicine was well accepted and may be viewed as a powerful tool to offer remote medical care to AG patients during health emergencies making infeasible face-to-face outpatients visits due to social distancing and lockdown to control the spread of pandemic infection.

Disclosure: Nothing to disclose

P1452

GASTROINTESTINAL SYMPTOMS DURING COVID-19 LOCKDOWN: INTERNET-BASED, CROSS-SECTIONAL STUDY OF THE BULGARIAN POPULATION

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Introduction: The COVID-19 pandemic progresses across the globe at pace, resulting in the need to “lockdown” the populations of many countries. Quarantine with social distancing has greatly reduced the transmission of COVID-19, however, there is no data whether this important life event stress and / or the fear of infection impacts on the prevalence of gastrointestinal (GI) symptoms.

Aims & Methods: This cross-sectional, population-based study aimed to evaluate the prevalence of GI symptoms during a lockdown, to compare the findings with similar data acquired prior to the onset of the COVID-19 pandemic and to associate the results with stress and anxiety. Two internet-based health surveys were sent to Bulgarian adults, 18 to 65 years old. The first collected data from May to August 2019, the second from March to May 2020. Individuals were invited to complete an online questionnaire on general and GI health.

The aim of the study was not explicitly stated. No personal identification data was collected (fully anonymized). Both surveys collected data on socio-demographic and behavioral characteristics, diagnostic questions based on Rome IV criteria to assess functional abdominal pain, irritable bowel syndrome (IBS), functional dyspepsia (FD), heartburn, and milk intolerance. The second survey also included the perceived stress scale 4 (PSS-4) and the general anxiety disorder - 7 (GAD-7) questionnaires.

Results: Data was collected from 2876 individuals: 1896 in the first (mean age = 35.5 years, SD = 11.7, 73.1% females) and 980 non-identical subjects in the second survey (mean age = 40.5 years, SD = 12.6, 74.3% females). Overall GI symptoms were reported by 68.9% during the COVID-19 lockdown compared to 56.0% under normal circumstances the previous year ($p < 0.001$). The prevalence of IBS-like symptoms was higher during lockdown compared to data collected in 2019 (26.3% vs. 20.0%; $p < 0.001$). Similar results were obtained for FD-like symptoms (18.3% vs. 12.7%; $p < 0.001$), abdominal pain at least once a week (48.5% vs. 40.0%, $p < 0.001$), heartburn (31.7% vs. 26.2%, $p = 0.002$) and milk intolerance (43.5% vs. 37.8% $p = 0.004$).

Many individuals reported multiple symptoms. PSS=4 was associated with FD-like symptoms ($p = 0.045$) and abdominal pain ($p = 0.013$). GAD-7 was associated with IBS-like symptoms ($p < 0.001$), FD-like symptoms ($p < 0.001$), abdominal pain ($p < 0.001$), heartburn ($p < 0.001$) and milk intolerance ($p < 0.001$).

Conclusion: Overall GI symptoms were significantly more prevalent in the population during the COVID-19 lockdown than under normal circumstances the previous year. This effect is likely due to an increase in functional GI complaints as indicated by significant rise in the prevalence of IBS and FD-like symptoms. Anxiety was associated with the increased

prevalence of all GI symptoms. High levels of stress had an impact mainly on abdominal pain and FD-like symptoms. Gastroenterologists should be aware of the impact that anxiety and stress has on the prevalence of functional abdominal symptoms, especially during the unique circumstances of the COVID-19 lockdown.

Disclosure: Nothing to disclose

P1453

GASTROINTESTINAL MANIFESTATIONS OF COVID 19: PREVALENCE AND TEMPORAL CHARACTERISTICS OF DIARRHOEA, VOMITING AND LIVER DYSFUNCTION IN COVID-19 INPATIENTS AT A UK GENERAL DISTRICT HOSPITAL

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Introduction: COVID-19 is a novel infectious disease caused by SARS-CoV-2 virus which can manifest with multisystemic sequelae. Gastrointestinal (GI) disturbances, such as diarrhoea and vomiting, have been reported in patients with COVID-19 but the prevalence is not clearly known, ranging from 1%-36% of patients in published studies [1].

There is potential for occult faecal-oral transmission as patients with GI symptoms appear to maintain faecal SARS-CoV-2 RNA load beyond the point of symptomatic resolution of COVID-19. GI manifestations of COVID-19 may affect patient outcomes [2, 3].

Liver function is also thought to be affected in the disease course with a case series reporting a 29% prevalence of liver dysfunction in COVID-19 patients. The implications of COVID-19 induced liver injury are yet to be investigated.

Aims & Methods: We aimed to determine the prevalence of GI symptoms and liver dysfunction in our local COVID-19 positive inpatient population. We investigated the temporal associations between COVID-19 onset and GI disturbance. This was a single centre retrospective observational study enrolling all consecutive inpatients with RT-PCR confirmed COVID-19 (10/03/2020 - 17/04/2020) who completed full hospitalisation. We excluded patients below 18 years of age and patients with no data on GI symptoms or liver function tests.

We used Electronic Health Records (EHR) to collect data on GI disturbance, blood results, care requirements and outcomes (requirement for Continuous Positive Airway Pressure ventilation, Intensive Treatment Unit admission or death).

Results: 260 patients (mean age: 67.1 years old, 45% female) were included in the study. 66 (25.4%) patients had diarrhoea and 33 (12.7%) had vomiting in this. The mean time to diarrhoea and vomiting onset was 4.9 days and 4.0 days from the COVID-19 symptoms onset, respectively. 16 patients (6.2%) had diarrhoea and 12 patients (4.6%) had vomiting on the first day of their COVID-19 illness. 39.4% of patients with diarrhoea developed this symptom during their inpatient stay. 218 (83.9%) patients received antibiotics during admission.

Liver function tests (LFTs) were deranged in 25 (10.1%) patients (defined as peak alanine aminotransferase (ALT) three times the upper limit of local normal). The average time from admission to ALT peak was 5.4 days and from COVID-19 symptoms onset to ALT peak 12.4 days.

Higher C-reactive protein (CRP) level was independently associated with diarrhoea (152 vs 180, $p < 0.019$) and deranged LFTs (152 vs 215, $p = 0.047$).

	Deranged liver function (N=25)	Normal liver function (N=223)	P value
Female (N [%])	13 [52.0]	96 [43.0]	0.461
Age (mean [SD])	65.9 [14.9]	67.2 [18.6]	0.551
Peak C-reactive protein (mean in mg/L [SD])	215 [154]	152 [123]	0.047
Length of stay (days [IQR])	11.2 [7-15]	8.6 [3-10]	0.001
ITU admission (N [%])	7 [28.0]	15 [6.7]	<0.001
Mortality (N [%])	7 [28.0]	78 [35.0]	0.517

[Characteristics of COVID-19 inpatients with and without deranged liver function]

Conclusion: Patients admitted with COVID-19 presenting to our centre frequently complain of diarrhoea and vomiting. The majority of patients have diarrhoea pre-admission but more than one third develop it whilst in hospital. Diarrhoea is associated with higher CRP. The prevalence of significantly abnormal LFTs is about 1 in 10. Diarrhoea tends to present early in the disease course (4 days) whilst the peak LFT derangement occurs at 12.4 days. Clinicians should consider COVID-19 testing in patients presenting with otherwise unexplained GI symptoms.

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Disclosure: Nothing to disclose

P1454 WITHDRAWN

P1455

TRANSNASAL ENDOSCOPY DURING COVID-19 PANDEMIC: A SAFE AND FEASIBLE ALTERNATIVE

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Introduction: COVID-19 can be transmitted via aerosolized viral particles. Therefore, EGD is considered a high risk procedure and most societies recommend postponing procedures until the pandemic is over. Transnasal endoscopy has potential advantages over peroral gastroscopy in terms of aerosol transmission, sedation, costs and management of patients in the recovery room.

Aims & Methods: The aim was to evaluate the efficacy and safety of transnasal endoscopy (TE) for upper gastrointestinal endoscopy during the COVID-19 pandemic.

During the acute phase of the COVID-19 pandemic, patients undergoing EGD were prospectively scoped with transnasal endoscopy. A questionnaire was used to assess patients', physicians' and nurses' preferred choice of method, psychological aspects, preference for a method to future examinations, and tolerability. In addition, feasibility, quality of biopsies, sedation, and time in the recovery room were assessed.

Results: A total of 59 patients were prospectively included. Technical success rate of TE was 98% and diagnostic success rate was 100%. Patients', physicians' and nurses' satisfaction rates were rated as being highest in 95%, 98%, and 98% of cases. Sense of security related to potential COVID-19 transmission was rated as being highest in 98%, 100% and 100% for patients, physicians and nurses, respectively. Sedation was required in 33% of patients. Biopsies were obtained in all cases and 100% of them showed adequate quality for subsequent histopathological workup. 75% of patients could be discharged home directly after the procedure, while 25% were observed for a mean time of 25 minutes in the recovery room. 93% of patients would prefer transnasal endoscopy as the first choice for the next EGD procedure. Epistaxis occurred in 2 patients. No additional complications were assessed during the course of the study.

Conclusion: Transnasal endoscopy is a promising technique for upper gastrointestinal endoscopy during the COVID-19 pandemic. The procedures were safe, well tolerated and associated with a high level of patients, physicians and nurse satisfaction. Most procedures were feasible without sedation, resulting in short recovery times and fewer staff members attending the procedures thereby limiting their exposure time in a potential higher risk environment. Transnasal endoscopy should be considered as first line diagnostic option for patients requiring EGD during the COVID-19 pandemic. The study is ongoing and final results will be presented at UEGW.

Disclosure: Nothing to disclose

P1456

PROS AND CONS OF IMPLEMENTATION OF STRATEGIC RESPONSE TO COVID-19 PANDEMIC IN ENDOSCOPY UNIT: SINGLE TERTIARY CENTER EXPERIENCE

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Introduction: In March 2020, the WHO declared COVID-19 as a global pandemic. It was clear that this rapidly evolving virus would have a broad impact on clinical care and GI practice which is our main concern.

Aims & Methods: We aimed to describe Mansoura University Endemic Hepatology and Gastroenterology Department experience in endoscopy unit preparation for COVID-19 pandemic and patient care during this unprecedented time.

In this descriptive study, based on the WHO recommendations, international guidelines, national policy of the Egyptian Ministry of Health and capabilities of our institute, we promptly developed a response strategy to deal with the situation. This strategy outlined 4 crucial issues to be addressed:

- 1-Development of competent surveillance team to observe, screen and notify the relevant authorities to take the WHO recommended actions.
- 2-Development of action plan to prepare the hospital for the anticipated gush of suspected cases with a well equipped health isolation area, operated by dedicated medical teams to deal with this cohort of patients. Upon confirmation of COVID-19 status, the cases are transferred to the quarantine hospitals to receive required health care service.
- 3-Starting intensive infection control course to ensure spreading the awareness among health care workers (HCWs) regarding the adherence to infection control measures.
- 4-Adoption of "Minimizing policy" to reduce the number of patients attending the endoscopy unit for non-urgent reasons.

Results: Through collaborative efforts and lessons learnt from other institutes worldwide, our surveillance team was able to early recognize the burden of suspected cases and take the proper actions to deal with the problem.

Being one of the biggest hospitals in Egypt in terms of capacity, our institute was able to reduce the pressure on other nearby health care facilities and to redistribute the flow of patients in a manner compatible with the degree of readiness. Throughout 1203 endoscopies performed between August 2019 and April 2020, endoscopy room capacity was significantly reduced between these 2 months respectively (n=196; 16.3 % vs n=8; 0.06% p<0.0001).

Knowing that the average hospital cost of diagnostic upper/lower GI endoscopy per patient in our institute is ~25 US dollars, our minimizing strategy seemed to be cost-effective in achieving significant reduction in endoscopy monthly costs between pre (August:December 2019) and post (January:April 2020) COVID-19 era respectively (n=25175; 83.7% vs n=4900; 16.3% p<0.0001).

Satisfaction of HCWs with the quality of personal protective equipment and infection control training programs reached 93% and 95% respectively through survey involving all HCWs in our hospital. Additionally, wise HCWs involvement in the work process through 2 weeks on, 2 weeks off strategy, has achieved its ultimate goal not only in terms of minimizing the risk of infection but also maintaining the optimum level of psychological health which is substantially valuable during these times.

One unpleasant finding in this study is that degree of satisfaction with endoscopy training among 22 trainees was significantly low (n=6;27.3% vs n=16;72.7% P=0.0029), measured by satisfaction scale questionnaire ranging from 0 (not satisfied at all) to 3 (very satisfied). This could be explained by significant reduction of the number of elective endoscopies which represent the core of endoscopy training schedules.

Conclusion: Development of a design taking into account the infrastructure, manpower and redistribution of resources, is the key factor to adequately respond to a global crisis like COVID-19.

Disclosure: Nothing to disclose

P1457

LEADING FACTORS OF LIVER INJURY AMONG HOSPITALIZED PATIENTS WITH COVID-19: EXPERIENCE FROM A COVID-19 REFERRAL HOSPITAL

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Introduction: Although COVID-19 is predominantly a disease of the respiratory tract, liver injury manifesting as abnormal liver function tests (LFTs) may occur in up to one third of patients; its significance is as yet unclear.

Aims & Methods: The aim of this study is to retrospectively identify factors that attribute to liver injury among hospitalized patients with COVID-19 in our COVID-19 referral center between 13th March and 5th May 2020. We analyzed data from 60 consecutive hospitalized patients with confirmed COVID-19. All patients received hydroxychloroquine 400mg for 5 days and azithromycin 500mg for 7 days. Patient age, gender, co-morbidities, and duration of in-hospital (including Intensive Care Unit-ICU) stay were recorded. Essential laboratory tests (complete blood count, CRP, ESR, LFTs, BUN, creatinine, and electrolytes) were also recorded on admission and during hospitalization. Patients were divided into two groups based on

the presence or absence of liver injury (elevation of transaminases and/or cholestatic enzymes). Univariate logistic regression analysis was performed to identify which factors were associated with liver injury; this was followed by multivariate logistic regression analysis which included the previously tested variables with p<0,2 and results were considered statistically significant when p<0,05.

Results: Of 60 patients, 31(51,7%) patients developed liver injury. On the univariate analysis, risk factors associated with liver injury were admission in ICU (p=0,005) and length of hospital stay (p=0,007). No statistically significant association was found for age (p=0,06), gender (p=0,155), co-morbidities (p=0,178), white blood cell count (p=0,407), percentage of lymphocytes (p=0,267) and absolute number of lymphocytes (p=0,813).

On the multivariate analysis which also included variables with p<0,2 (age, sex and co-morbidities) only admission in ICU (p=0,027) and the length of hospital stay (p=0,048, C.I.=1,001-1,212) were shown to be the only risk factors independently associated with liver injury.

The odds ratio (OR) for developing liver injury in ICU admitted patients was 12,34. Prolonged hospitalization increased the risk for developing abnormal LFTs, as patients with abnormal LFTs had a median hospitalization of 15 (IQR=8-19) days compared to patients with normal LFTs 7 (IQR=2,75-11,75) days (p=0,002).

	Univariate Analysis				Multivariate Analysis			
	OR	95% C.I.		p	OR	95% C.I.		p
		Lower	Upper			Lower	Upper	
Age	1,035	0,999	1,072	0,06	1,028	0,980	1,078	0,254
ICU	9,871	2,027	48,081	0,005	12,340	1,323	115,078	0,027
Gender	0,450	0,150	1,352	0,155	0,651	0,149	2,836	0,567
Absolute number of Lymphocytes	1,000	0,999	1,001	0,813				
Length of hospital stay	1,116	1,030	1,209	0,007	1,102	1,001	1,212	0,48
Co-morbidities	0,446	0,138	1,443	0,178	0,800	0,125	5,124	0,814

[Univariate and Multivariate Analysis of liver injury to risk factors]

Conclusion: Liver injury in COVID-19 patients is associated with prolonged hospitalization and especially admission to ICU. This implies that systemic inflammation and/or sepsis rather than the viral infection per se or the treatment play a fundamental role developing liver injury.

Disclosure: Nothing to disclose

P1458

HEALTH RISK AND ACCESS TO HEALTH CARE PERCEPTION AMONG IBD PATIENTS DURING COVID-19 LOCKDOWN

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Introduction: COVID-19 epidemic changed the way of providing health care to chronically ill patients. In countries with high incidence of COVID-19 significant relocation of health care resources had to take place whilst in low incidence countries the lockdown was the main factor limiting the access

to standard care. Regarding the increased health risks, in addition to limited access to health care, immune compromised IBD patients may also carry an increased risk of COVID-19 infection although preliminary data from high incidence countries do not support this concern. In the period of COVID-19 epidemic and the lockdown, IBD patients may thus feel vulnerable, be at risk of psychological disorders and ensuing issues with the adherence to IBD therapy.

Aims & Methods: The aim of this study was to assess IBD patients' perception of COVID-19-related health risk and access to health care during lockdown. During the last two weeks of April 2020, 5 to 6 weeks after lockdown of Slovakia, IBD patients, members of Slovak Crohn Club were asked to fill out an online anonymous questionnaire. The questionnaire was developed by IBD specialists, in cooperation with patients' representative of Slovak Crohn Club and an IBD-oriented psychologist. The questions aimed at following issues: 1. specific concerns of IBD patients regarding the health risk related to COVID-19 epidemic; 2. IBD therapy adherence during the epidemic; 3. experience of IBD patients with medical care during the lockdown.

Results: In total, 136 patients responded, majority were women (60%) and patients with the duration of the disease for over 5 years (93 pts, 63%). Twenty-three percent of the patients were between 18 and 30 years old, 38% were 30 to 45 years old, 26% were between 45 to 60 and only minority of 13% were more than 60 years old. Nearly half of the patients (65 pts; 48%) were on biologics, 40% (55 pts) were using thiopurines monotherapy, minority were on combined immune suppression (28 pts; 21%) or systemic corticosteroids (12 pts; 9%).

Majority of patients (110 pts; 81%) considered themselves to be more at risk for complicated COVID-19 infection course compared to healthy population. With regards to the risk of relapse vs. the risk of contracting infection, half of the patients (65 pts; 48%) reported to feel primarily threatened by infection while only 19% (25 pts) perceived higher risk of relapse; 33% (45 pts) were not able to answer this question. With regards to anxiety and depression, 56% of patients felt more often or significantly more often anxious since the beginning of the lockdown while 43% of patients experienced more often or significantly more often the symptoms of depression. Only few patients (7; 6%) reported to have decreased the dose or to have stopped the immune suppressive medication out of fear for infection, the remaining patients (94%) continued the medication without any change. Only 15% (21pts) of patients had worsening of IBD symptoms since the beginning of the lockdown. All but one of these patients were able to reach their treating gastroenterologist, the majority were offered telephonic consultation (12; 63%).

Conclusion: During the COVID-19 epidemic and lockdown, IBD patients feel more at risk for infection than for IBD relapse and half of them report anxiety and symptoms of depression. Despite the fear for more complicated course of infection, the vast majority of patients continue their immune suppressive medication. During the lockdown, the health care is shifted towards telemedicine.

Disclosure: Nothing to disclose

P1459

THE IMPACT OF A DEDICATED INFLAMMATORY BOWEL DISEASE CONTACT CENTER ON CLINICAL OUTCOME OF PATIENTS DURING THE COVID 19 OUTBREAK

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Introduction: Given the significant interruption of elective activity in the COVID-19 era and thereby the resetting of clinical priorities, a reorganization of health care for patients with inflammatory bowel disease (IBD) is warranted.¹

Aims & Methods: In the COVID-19 context, we aimed to investigate the impact of an IBD dedicated contact center service (CCS), held at an Italian tertiary academic centre, on IBD team reorganization and on the major clinical outcomes.

We conducted an observational study evaluating the CCS activities offered to 3680 IBD patients followed-up at our IBD unit by comparing the pre COVID-19 (January-February 2020) to the COVID-19 era (March-April 2020) and to the same period of the year 2019. We further analysed the following clinical outcomes: the number of intravenous biological therapy, hospitalizations and surgical procedures in the same three periods. Data were analysed by STATA statistical software. The differences between means before and after COVID-19 era were determined using the two-sample Student's t-test and chi-square when appropriate. All differences were considered significant in presence of $p < 0.05$.

Results: In the COVID-19 period, our CCS received a total of 971 contacts in comparison to 881 related to the two months pre-COVID-19 (26% vs 23%; $p=0.02$), while we registered a decrease of CCS activity (26% vs 33%; $p < 0.01$) in respect to the same period of 2019. During the COVID-19 outbreak the majority (65,1%) of inbound calls aimed to talk with a physician belonging to our IBD team, 23,7% of patients called to ask logistics information, while 11,1% wanted to change their visits date or book new appointments. Among all the requested information, 66% concerned COVID-19. With regard to the major clinical outcomes, no significant difference was detected in the rate of intravenous biological therapy pre- and during COVID-19 period (296 vs 307; $p=n.s.$); whereas comparing the number of intravenous biological therapy during the outbreak to the same period of 2019 we reported an increase rate of 19,4% (from 257 to 307; $p=n.s.$). In addition there was a significant reduction in terms of the rate of hospitalization before and during the COVID-19 periods (158 vs 96; 4% vs 2%; $p < 0.01$). Conversely, the rate of surgery did not differ significantly between pre-COVID-19 and during COVID-19 periods (10 vs 9; $p=n.s.$). Finally, regarding the patient's satisfaction, 95% of patients stated to be highly satisfied from CCS, while 5% moderately satisfied. As far as the feeling of relief concerned, 78% felt reassured and 21,8% more confident to interact with physicians using the CCS.

Conclusion: We are seeing the dawn of a new era of home patient management replacing follow up visits and controls. Our results can provide the basis for implement an IBD dedicated contact service in clinical practice in the post COVID-19 era. Hence, we can achieve high quality of care even at home for IBD patients.

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Disclosure: Nothing to disclose

P1460

SARS-COV-2 INFECTION OF THE INTESTINAL TRACT MODELLED IN HUMAN PLURIPOTENT STEM CELL-DERIVED INTESTINAL ORGANIDS

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Introduction: The COVID-19 pandemic, caused by beta-corona-virus SARS-CoV-2, has spread to over 180 countries worldwide and poses a severe health risk to the global population. While the most common symptoms are fever, cough and in severe cases pneumonia, about 10 % of patients also show a variety of gastrointestinal symptoms like diarrhoea, vomiting and abdominal pain. Additionally, high titers of the virus can be detected in faeces of patients, even long after nasopharyngeal swabs are tested negative.

Aims & Methods: It is therefore of high interest to not only investigate the viral effects on the lung, but also to take a closer look at the effects of SARS-CoV-2 in the gastrointestinal tract. Immune histological stainings of different tissues and organs of the gastrointestinal tract showed strong expression of the viral entry receptor ACE2 especially in the small intestine. To investigate whether the virus is able to infect and replicate in intestinal tissue, human stem cell derived intestinal organoids were used. Compared to intestinal cell lines cultivated in monolayer, organoids have the advantage of forming complex 3D structures with different compartments and generating not only one but all cell types of the intestine.

Results: Just like in primary tissue, a strong expression of ACE2 was detectable in intestinal organoids. Organoids were infected with wildtype SARS-CoV-2 and analysed after different time points for infection. 24 h after infection, viral spike protein was already detectable in the organoids, however only in a small proportion of cells. After 48 h the virus had spread throughout around 70 % of the cells, indicating that it cannot only infect but also successfully replicate in intestinal organoids. Infected cells showed signs of cell death and the morphology of organoids was visibly disturbed by the presence of the virus.

Conclusion: The data suggest that intestinal organoids can be used as a tool to investigate the effects of SARS-CoV-2 infection in the gastrointestinal tract *in vitro* and to test potential compounds and inhibitors that might be able to inhibit viral infection or replication.

Disclosure: Nothing to disclose

P1461 WITHDRAWN

P1462

A POPULATION-BASED STUDY ON COVID-19 AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASES: PRELIMINARY RESULTS FROM THE DANISH COVID-IBD DATABASE

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Introduction: Patients with immune-mediated diseases (IMDs) are postulated to be at increased risk of infection by SARS-CoV-2, a novel virus giving rise to COVID-19 which has rapidly become a global health emergency. However, data on the risk profile of patients with inflammatory bowel diseases (IBD including Crohn's disease (CD) and ulcerative colitis (UC)) are scarce.

Aims & Methods: We aimed to conduct a prospective population-based study including all patients with co-occurring IBD and COVID-19 in Denmark. The objectives were to characterize these patients, as well as their short-term outcomes in terms of hospital admissions, admissions to intensive care units, requirements of ventilators and mortality. The patients were identified both manually at all IBD ambulatory centers as well as by electronic diagnosis codes. Clinical remission of IBD was defined as Harvey Bradshaw Index ≤ 4 or Simple Clinical Colitis Activity Index ≤ 2 , biochemical remission was defined as C-reactive protein (CRP) < 5 or f-Calprotectin < 200 and endoscopic remission was defined as Mayo Endoscopic score ≤ 1 . In addition, we estimated the prevalence of COVID-19 among patients with IBD through surveys sent to members of the Danish IBD patient association (CCF).

Results: Four patients with IBD were tested positive for SARS-CoV-2 in a survey answered by 2000 patients with IBD, which is equal to a prevalence of COVID-19 of 0.2%. In the nationwide database, a total of 23 patients had co-occurring IBD and COVID-19 and all were enrolled in this study. Most of these patients (15/23) were living in the Capital Region of Denmark. CD and UC appeared equally in the cohort and the median age at diagnosis of COVID-19 was 46 (IQR 39-59). The disease localization of CD was mostly confined to the colon (6/11), while 5/12 of the patients with UC had proctitis. In total, 12/23 patients were in clinical remission at COVID-19 diagnosis, while 14 patients and five patients were in biochemical and endoscopic remission, respectively.

Every fourth of the patients were non-smokers (6/23) and most were overweight with a median body mass index of 29 (22-30). A total of 12 patients received IMS including azathioprine (7) and biologic therapies (adalimumab: 4, infliximab: 2 and vedolizumab: 2). In addition, seven patients had undergone colectomy.

A large proportion of the patients had other co-occurring IMDs including asthma (3), spondyloarthropathy (1), type 1 diabetes (1), psoriasis (1) and celiac disease (1). A total of four patients required hospitalization due to COVID-19 with a median admission length of 23 days (11-35), of which

two patients required admission to an intensive care unit with treatment with either non-invasive ventilator or mechanical ventilator. The risk of hospital admission did not seem to be associated with the treatment with IMS as only half of the patients received these therapies. Lastly, one elderly patient with co-occurring asthma among our cohort died due to COVID-19.

Conclusion: From this ongoing population-based study, we report a low prevalence of 0.2% of COVID-19 among patients with IBD in Denmark. Our findings are in line the current literature but might be biased due to different screening strategies over time in Denmark. We notice that a high proportion of patients with COVID-19 and co-occurring IBD were obese, had a prior colectomy and required hospitalization and admission to an intensive care unit. This does not seem to be associated with the IBD-related immunosuppressive therapies, and the high proportions could be due to the low sample size.

Disclosure: Nothing to disclose

P1463

COVID-19 AND INFLAMMATORY BOWEL DISEASE: PREVALENCE, RELATIONSHIP WITH IMMUNOSUPPRESSIVE THERAPIES AND MENTAL WELL-BEING. A NATIONWIDE DANISH SURVEY

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Introduction: Patients with inflammatory bowel diseases (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) are susceptible to several infectious diseases. SARS-CoV-2 is a novel virus giving rise to COVID-19 which has rapidly become a major health emergency worldwide.

Aims & Methods: We aimed to investigate the prevalence of COVID-19 among members of the Danish IBD patient association (CCF) and retrospectively explore the possible relationship between IBD-related immunosuppressive therapies and the risk of developing COVID-19.

In addition, we investigated patient compliance hereof in relation to perceived stress due to concerns about COVID-19, assessed by the validated Perceived Stress Scale (PSS). PSS-scores < 14, 14-26 and >26 were considered low, moderate and high grades of perceived stress, respectively. We also investigated information sources related to the COVID-19 pandemic. The assessments were conducted through surveys distributed by CCF as well as a major patient-oriented information website.

Results: Between April 6 and May 8, 2020, a total of 2017 patients participated in the survey of which 17 were excluded from the study due to absence of IBD diagnosis. Among 2000 IBD patients, we found a total of four patients, all women aged 46 (IQR 38-49), who were tested positive for SARS-CoV-19 (three with CD and one with UC) reflecting a COVID-19 prevalence of 0.2% among our patient population.

Overall, 672 (33.6%) IBD patients received biologic therapies, 592 (29.6%) received immunomodulators (azathioprine, mercaptopurine or methotrexate) and 56 (2.8%) received systemic steroids. These therapies were not over-represented among SARS-CoV-19 positive IBD patients but they could not be assessed statistically due to the small sample size.

Overall, IBD patients were compliant with the IBD-related therapies as only 30 (1.5%) discontinued the treatments on their own, while 67 (3.4%) and six (0.3%) patients discontinued their therapy after agreement with a gastroenterologist or general practitioner, respectively. In general, IBD

patients sought for COVID-19 related information using the Danish health authorities (80.4%), patient associations (53.8%), hospital departments (23.4%) and social media (22.3%). Only 5.6% and 4% sought information through their nurse or the Danish Society of Gastroenterology and Hepatology, respectively. The outbreak of COVID-19 seems to affect IBD patients' mental health as 52.8% and 7.2% had a moderate or high level of stress according to PSS, respectively, while 40.0% experienced a low grade of stress since the outbreak of COVID-19. Patients receiving biologic therapies were at higher risk of having a high level of stress (10% vs 6%, Chi squared test $p < 0.001$) or moderate to high levels of stress (65% vs 56%, $p < 0.001$). However, patients with high PSS-scores were not at increased risk of discontinuing their IBD-related treatment ($p = 0.85$) which is in line with the current recommendations.

Conclusion: Patients with IBD do not seem to be more susceptible to COVID-19 than the general population and immunosuppressive therapies do not seem to modulate this risk. However, due to different screening strategies in Denmark since the outbreak of COVID-19, our results may be biased and require further elucidation in a prospective study. Even though patients with IBD seem to be compliant with their IBD-related treatment as encouraged in the guidelines, clinicians caring for these patients must not neglect the concerns and mental well-being of IBD patients, especially those in biologic therapies.

Disclosure: Nothing to disclose

P1464

TNFA-ANTAGONIST USE AND MUCOSAL INFLAMMATION ARE ASSOCIATED WITH INCREASED INTESTINAL EXPRESSION OF SARS-COV-2 HOST PROTEASE TMPRSS2 IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become pandemic. Viral entry is dependent on angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2)^[1]. Recent studies show cell-type specific co-expression of ACE2 and TMPRSS2 in the gastrointestinal tract, in addition to the respiratory tract, and suggest that the intestinal epithelium supports viral entry^[2,3]. Intestinal expression of ACE2 and TMPRSS2 in patients with inflammatory bowel disease (IBD) may depend on local inflammatory activity and the degree of epithelial damage^[4]. Indeed, patients with active IBD seem to be at risk for negative outcomes of COVID-19^[5]. The question remains what specific factors contribute to these negative outcomes.

Aims & Methods: This study aimed to explore the effects of intestinal inflammation, immunomodulating drugs, age, sex and BMI on the intestinal expression of ACE2 and TMPRSS2 in patients with IBD. We performed bulk RNA sequencing of 92 ileal and 199 colonic snap frozen mucosal biopsies from 168 patients with IBD. Genotypes were obtained using imputed Global Screening Array data and whole exome sequencing. We analysed clinical data regarding the use of immunomodulating drugs, age, sex, and BMI. Mucosal inflammation status was endoscopically assessed at time of

biopsy. Multivariate linear mixed regression analyses were performed to assess the effects of clinical factors (including intestinal mucosal inflammation, use of immunomodulating drugs, age, sex, and BMI) on intestinal gene expression levels of *ACE2* and *TMPRSS2*. In addition, we assessed the effects of host genetic variation on gene expression (cis-expression quantitative trait loci).

Results: *ACE2* and *TMPRSS2* are differentially expressed in the ileal mucosa in inflamed biopsies. Interestingly, expression of *ACE2* was lower, and expression of *TMPRSS2* was higher in inflamed tissue compared to non-inflamed tissue, independent of medication use, age, sex, and BMI ($P = 3.0 \times 10^{-5}$ and $P = 5.9 \times 10^{-9}$, respectively).

In addition, we found increasing *TMPRSS2* expression with age and in ileal biopsies of patients using Tumour Necrosis Factor alpha (TNF α)-antagonists ($P = .04$ and $P = 5.6 \times 10^{-6}$, respectively). Because aminosaliculates were only used in the context of ulcerative colitis, we assessed the influence of aminosaliculates in colonic tissue only, and observed an increased *TMPRSS2* expression in colonic biopsies ($P = .02$). Male sex was associated with increased *TMPRSS2* expression in intestinal (ileal and colonic) biopsies ($P = .02$). The use of thiopurines or steroids was not associated with differential expression of *ACE2* or *TMPRSS2*. Furthermore, host genetic variation was not associated with differential expression of *ACE2* or *TMPRSS2*.

Conclusion: *TMPRSS2* is the primary host protease that mediates cellular entry of SARS-CoV-2. Currently, little is known about COVID-19 in the context of IBD and the use of immunomodulating drugs like TNF α -antagonists.

We report increased expression of *TMPRSS2*, but not *ACE2*, in intestinal mucosal biopsies of older patients, of male patients, with mucosal inflammation, and in patients using TNF α -antagonists or aminosaliculates. This in turn might contribute to a more severe course of COVID-19, but this hypothesis is yet to be confirmed in follow-up studies.

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Disclosure: Nothing to disclose

P1465

SUCCESSFUL COPING WITH SARS-COV-2 INFECTION OF ADULTS COELIAC DISEASE PATIENTS ASSESSED BY TELEMEDICINE

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Introduction: Coeliac Disease (CD) patients may have an increased risk for bacterial and viral infection associated to defective splenic function, excess of osteopontin and vitamin D deficiency¹⁻³. No data are currently available on new SARS-CoV-2 infection occurrence amongst CD patients. SARS-CoV-2 pandemic is having a drastic impact on routine healthcare.

Telemedicine was proposed as an expedient instead of face-to-face visits in order to properly establish the management of pts with chronic diseases during pandemic⁴.

Aims & Methods: The aim of this study was to use telehealth to evaluate pts' risk perception and quality of life (QoL) changes related to pandemic, impact of SARS-CoV-2 pandemic on gastrointestinal (GI) symptoms and gluten-free diet (GFD) adherence in a cohort of CD pts. This is a cross-sectional study on CD pts diagnosed in a Central Italy academic referral center for CD. Inclusion criteria were: 1) adults with diagnosis of CD; 2) GFD lasting at least 1 year from CD diagnosis; 3) the last outpatient visit within the last 12 months; 4) absence of refractory CD. Risk of SARS-CoV-2 infection and respiratory symptoms appeared in a period lasting from 1st January 2020 to the telephone interview time-point were collected by a specific questionnaire, SARS-CoV-2-related QoL changes and risk perception by a verbal rating scale (0-10 scale). Persisting (already present at the previous visit) or new (onset during the COVID-19 pandemic) GI symptoms were evaluated by a standardized questionnaire⁵, GFD adherence by Biagi score⁶.

Results: Of the 165 CD includible pts, 111 (67.3%, median age 41, 18-76 years; F:M ratio=2:1) adhered to telehealth interview. No verified cases of SARS-CoV-2 infection were identified in the CD cohort. 17.1% pts reported respiratory symptoms during pandemic: fever ($>37.5^{\circ}\text{C}$) in 9%, cough in 5.4% and anosmia/ageusia in 1.8%. With regard to life-style changes due to lockdown, 85.6% stayed at home, 9.9% had high-risk and 4.5% low-risk jobs. Concerning the self-perception of QoL during pandemic, 79.3% perceived no substantial variations, 6.3% declared an improvement and 14.4% a worsening of their QoL than before the pandemic. 55.9% did not perceive any type of risk during pandemic.

Of the 11 CD pts (17.1%) who perceived a high COVID-19 related risk (7-to-10 at 0-10 scale), 8 reported high-risk jobs. Concerning GI symptoms, 29.7% of pts stated GI persisting symptoms, mostly represented by abdominal pain, bloating and episodic diarrhoea, while 11.7% complained new GI symptoms during pandemic, mainly mild or self-limiting diarrhoea and dyspepsia not requiring pharmacological treatment (gender and median age, $p=0.5$).

The proportion of CD patients with inadequate GFD (Biagi 0-2) decreased from 8% at the last face-to-face visit to 4.5% at telehealth interview ($p=0.4$). Most pts (72.1%) perceived the daily GFD management during SARS-CoV-2 pandemic as easier. Compared to the last face-to-face visit, more than half ($n=64$, 57.6%) of CD patients gained body weight (median 2Kg, range 1-9), while 6 (5.4%) complained a weight loss (median 2Kg, range 1-4).

Conclusion: The majority of interviewed CD patients successfully coped with SARS-CoV-2 pandemic. Few (1/10) CD patients experienced new self-limiting GI symptoms and the management of GFD was perceived as easier due to the stay-at-home strategy during pandemic. Telemedicine was well accepted by CD patients and it may be considered a useful tool to offer medical care to adult patients with CD in time of health emergency.

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Disclosure: Nothing to disclose

P1466

LIVER INVOLVEMENT IN COVID-19 PATIENTS - A MACHINE-LEARNING-ASSISTED ANALYSIS

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Introduction: The SARS-CoV2 pandemic poses a serious challenge to society and a threat to the global health care system. Physicians are forced to make fast decisions based on limited knowledge. By using machine learning techniques, we were able to exploit large amounts of data from intensive care unit (ICU) patients to derive patterns in the clinical picture of COVID-19 patients. Among other parameters, we identified liver to be an important indicator for a severe discourse of the disease.

Aims & Methods: We analyzed the recorded data of 56 COVID patients in the Intensive Care Unit including demographics, laboratory reports and high-frequency vital measurements such as ventilation and heart signals. A special focus was set on liver values namely glutamic-pyruvate transaminase (GPT), Bilirubin, alkaline phosphatase (ALP) and international normalized ratio (INR). By comparing this set of parameters with the baseline of a non-COVID patient group, we were able to define a simple yet effective severity score to classify liver involvements.

To calculate the score, each parameter is evaluated by the deviation to its defined normal value:

- Severity grade 1: deviation by 1,5-2x of normal value of GPT, Bilirubin and ALP and an INR of 1,15- 1,35
- Severity grade 2: deviation by 2-3x of normal value and 0,5 step of INR
- Severity grade 3: deviation by 3-4x of normal value and 0,5 step of INR
- Severity grade 4: deviation of 4 or more of normal value and 0,5 step of INR

Results: A cohort of 56 corona-virus positive patients were analyzed. All of the patients depicted signs of a liver involvement. 8 % show severity grade 1, 19 % severity grade 2 and 10 % severity grade 3. Of note, 60% of the cohort showed the highest severity grade 4. 26% of the patients which has the highest severity grade died and 44% of them are still at the hospital.

Conclusion: All of the 56 corona-virus positive patients in the cohort showed massive liver symptoms. There exists a clear correlation between elevated liver values and an increased mortality. In particular, 26 % of patients with a severity grade of 4 died. Thus, it is a challenging task for the future to unravel the molecular mechanisms of SARS-CoV-2 induced liver damage and to understand the connection of viral infection and liver involvement in detail.

Disclosure: Nothing to disclose

P1467

DRASTIC DECREASE OF URGENT ENDOSCOPIES OUTSIDE REGULAR WORKING HOURS DURING THE COVID-19 PANDEMIC IN THE PARIS AREA

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Introduction: The coronavirus 2019 (COVID-19) pandemic has significantly affected medical care. We surmise that the number of urgent endoscopies outside regular working hours in the Paris area decreased as a result. The objective of this study was to describe the observed number of acts during the 2020 mandatory period of home isolation, compared to the values in prior years and the expected value for 2020.

Aims & Methods: We performed a multicenter cohort study to investigate the practice of urgent endoscopy acts, outside regular working hours, in Paris and its surrounding suburbs, in the setting of the COVID-19 pandemic. We collected the number of endoscopies performed between January 17th and April 17th 2018, 2019 and 2020. We then collected clinical, endoscopic and outcome variables from the patients of years 2019 and 2020.

Results: From March 17th to April 17th (during home isolation), the number of acts was respectively of 147 in 2018, 137 in 2019, and 79 in 2020, lower than the expected number of 142 (-44.0%). In 2020, the number of endoscopies for suspected gastrointestinal bleeding (GIB), and findings of variceal and non-variceal bleeding decreased by 52.1%, 69.2% and 43.1% respectively, after a month of home isolation. In-hospital death rate were similar.

Conclusion: This study confirms that the urgent endoscopy caseload outside regular hours decreased nearly by half during the pandemic. Our results suggest a decreased number of endoscopies for suspected gastrointestinal bleeding, and findings of variceal and non-variceal bleeding.

Disclosure: Author M.C. is a consultant for Boston Scientific and Cook Medical. Author X.D. has acted as a consultant for Alfasigma, Bouchara Recordati, Boston Scientific, Fujifilm, Medtronic, and Pentax. Author X.D. is also cofounder and shareholder of company Augmented Endoscopy.

P1468

GASTROINTESTINAL MANIFESTATIONS OF COVID-19: A EUROPEAN COHORT STUDY

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Introduction: Infection due to SARS-CoV-2 virus is typically associated with a respiratory syndrome. Nevertheless, manifestations from different organs have been described, with gastrointestinal (GI) symptoms standing out, from early reports from China. However, data from European centres is lacking.

Aims & Methods: The aim of this study was to characterize the GI manifestations of patients with COVID-19 and their disease course. Patients admitted at our centre from 12th March to 30th April with positive RNA by real-time polymerase chain reaction from nasopharyngeal swab were included. Asymptomatic patients or those without symptom information were excluded. Clinical features, laboratory data and outcome (mechanical ventilation, intensive care admission or death) were analysed.

Results: A total of 201 patients were included (median age 71 [IQR 26] years; 56.2% male). Digestive symptoms were reported by 60 (29.9%) patients during the disease course, being part of the disease presentation in 34 (16.9%). The most frequent was diarrhea (n=36; 17.9%), followed by vomiting (n=22; 10.9%). Remarkably, 12 (6%) patients presented ageusia, a rather specific symptom. Patients with GI symptoms were younger (p=0.032), had higher haemoglobin levels (p=0.002) and lower C-reactive protein (p=0.045) and potassium (p=0.004) compared with patients without GI symptoms. There was no statistically significant difference between these two groups in terms of mechanical ventilation, intensive care admission or death (p=0.071). Regarding liver damage, AST was elevated in 131 (65.2%) patients and ALT in 126 (62.7%). When compared to patients without elevation, there was no statistically significant difference in terms of mechanical ventilation, intensive care admission or death (elevated AST p=0.118; elevated ALT p=0.442).

Conclusion: A significant portion of COVID-19 patients have digestive symptoms, mostly at presentation. This should be taken into account in order to keep a high level of suspicion, even when respiratory symptoms are absent, to reach an early diagnosis and set up infection control measures to control transmission rate. This subgroup of patients does not appear to have a more severe disease course.

Disclosure: Nothing to disclose

P1469

PRE-EXISTING LIVER DISEASES AND ON-ADMISSION LIVER-RELATED LABORATORY TESTS IN COVID-19: A PROGNOSTIC ACCURACY META-ANALYSIS WITH SYSTEMATIC REVIEW

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Introduction: Due to the pathogenic and contagious nature of SARS-CoV-2 and the high incidence of liver damage in these patients, an assessment of the liver function is urgently needed and the prognostic value of liver diseases needs to be determined. Moreover, the impact of underlying liver diseases on coronavirus disease-19 (COVID-19) progression and outcomes is unknown.

Aims & Methods: We aimed to perform a systematic search to evaluate the prognostic value of liver function and conditions on the clinical course of COVID-19. The study was registered on PROSPERO (CRD42020182902). We searched five databases between 01/01/2020 and 23/04/2020. Studies that reported on liver-related comorbidities and/or laboratory parameters in patients with COVID-19 were included. The main outcomes were COVID-19 severity, intensive care unit (ICU) admission, and in-hospital mortality. Analysis of predictive models hierarchical summary receiver-operating characteristic (HSROC) was conducted with a 95% confidence interval (CI).

Results: Fifty studies were included in the meta-analysis. High specificity was reached by acute liver failure caused by COVID-19 (0.94, CI: 0.71-0.99), platelet count (0.94 CI: 0.71-0.99) in the case of mortality; chronic liver disease (CLD) (0.98, CI: 0.96-0.99), platelet count (0.82, CI: 0.72-0.89) in the case of ICU requirement; CLD (0.97, CI: 0.95-0.98), chronic hepatitis B infection (0.97, CI: 0.95-0.98), platelet count (0.86, CI: 0.77-0.91), alanine aminotransferase (ALT) (0.80, CI: 0.66-0.89) and aspartate aminotransferase (AST) (0.84, CI: 0.77-0.88) activities considering severe COVID-19. High sensitivity was found in the case of C-reactive protein (CRP) for ICU requirement (0.92, CI: 0.80-0.97) and severe COVID-19 (0.91, CI: 0.82-0.96).

Conclusion: On-admission platelet count, ALT, AST activity and CRP concentration, and presence of acute and chronic liver diseases predicted severe course of COVID-19. To highlight, acute hepatic failure induced by SARS-CoV-2 infection plays an important role in the prediction of mortality.

Disclosure: Nothing to disclose

P1470

ESTIMATED EFFECTS OF SCREENING DELAY DUE TO SARS-COV-2 PANDEMIC ON COLORECTAL CANCER MORTALITY

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Introduction: The Sars-CoV-2 pandemic has had a sudden, dramatic impact on healthcare activities. In Italy, the implementation of colorectal cancer screening programs has had a significant effect on both incidence and mortality from the disease. However, since the beginning of the pandemic, colorectal cancer screening programs have been suspended across the country.

Aims & Methods: To forecast the impact of the pandemic on colon cancer screening program by building a model applying negative foreseeing primarily in function of the time-delays in access to colonoscopy and comparatively adjusted mortality for up-stage migration of patients. Estimates of the effects of time-delay on CRC stage and of stage on mortality were assessed by a meta-analytic approach.

Results: With a short delay of 0-3 months, 74% of the CRC are expected to be of stage I-II, while with a delay of 4-6 months we observe an increase in the stage I-II percentage (from 74% to 76%), and a corresponding decrease for stage III-IV ($p=0.068$). However, compared to 0-3 months delays, moderate (7-12 months) and large (>12 months) delays would lead to an increase in advanced CRC (from 26% to 29% and 33%, respectively; $p=0.008$ and $p<0.001$, respectively). The pooled survival rates at 5 years showed 0.85 for stage I-II and 0.39 for stage III-IV. A significant increase of deaths (+11.9%) was estimated when moving from a 0-3 months to a >12 months delay ($p=0.005$). Finally, we observed a significant change in mortality distribution by stage when comparing the baseline with the >12 months ($p<0.001$).

Conclusion: Our data indicates that delays beyond 4-6 months would negatively colon cancer screening by increasing disease mortality rates. This would occur due to the progressive shift of colorectal cancers from early stages to more advanced ones. In the view of possible future waves of Sars-Cov-2 or other pandemics, healthcare authorities need to urgently think on how to reorganize activities without breaking the workflow for high-impact diseases such as colorectal cancer.

Disclosure: Nothing to disclose

P1471

HOW AND HOW MUCH ENDOSCOPY PROFESSIONALS PROTECTED THEMSELVES AGAINST INFECTIONS, BEFORE THE COVID-19 PANDEMIC?

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Introduction: Now, with the COVID 19 pandemic, individual protection measures for endoscopic procedures are reinforced.

However, before this pandemic, personnel working in endoscopic environments were already exposure to blood, secretions, and other body fluids, with a risk infection by infectious microorganisms such as M. tu-

berculosis, hepatitis B virus, HIV, herpes simplex and enteric pathogens. Therefore, even before the pandemic, universal personal protection precautions should be applied during endoscopic procedures.

Aims & Methods: The aim of this study was to assess the level of individual protection measures of gastroenterologists and endoscopy nurses, before the COVID-19 pandemic.

Methods: 103 doctors and nurses, working in the endoscopy units from different hospitals in the country, responded to a 20-item online questionnaire. The questionnaire was distributed by the National Center for the Registration of Data in Gastroenterology (CEREGA - Portuguese Society of Gastroenterology).

Results: A total of 75 (72.8%) specialist gastroenterologists, 15 residents (14.6%) and 13 nurses (12.6%) responded. Most respondents worked in a public hospital (83%).

All professionals reported wearing gloves during endoscopic procedures and 63% reported wearing waterproof scrubs. However, 59% never or rarely wear a mask and 86% do not use face shields / eye protection during endoscopic procedures.

In all, 85% reported washing their hands, always or most of the time, before and after endoscopies. However, regarding the correct hand washing rules, only 9% reported always doing the washing properly, 27% did most of the time, 29% did it sometimes and 35% rarely or never did the correct hand washing rules.

There were no significant differences between professional groups.

82% self-assessed their level of protection at a 3-4 level (on a scale of 1 to 5), while 89% of them assessed their colleagues' level of protection at a level 2-3.

The main reasons given to justify non-adherence to individual protection measures were: carelessness of professionals, high cost and lack of accessibility of the equipment and their interference with the professional's skills/performance.

96% of respondents think that individual protection measures will improve after the pandemic.

Conclusion: As a result of our investigation, it was determined that, before the COVID-19 pandemic, the endoscopists and endoscopy nurses did not effectively apply the universal precautions against infectious risks faced during endoscopic procedures.

The COVID -19 pandemic seems to have raised awareness among professionals. Although there are some obstacles, they seem motivated to change attitudes in the future.

A future re-evaluation will be useful to find out if there has been a significant and permanent behavior change.

Disclosure: Nothing to disclose

P1472

EASING ENDOSCOPY DELAYS DUE TO COVID-19: APPLICATION OF SOCIETY GUIDELINES SIGNIFICANTLY FREES UP CAPACITY

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Introduction: In late 2019 the British Society of Gastroenterology (BSG) introduced updated guidance on the endoscopic surveillance of patients following resection of colonic polyps or colorectal cancer (CRC) (1). As with other surveillance programmes, the key stated aims were to reduce the incidence and mortality of CRCs in the post-polypectomy and post CRC-resection groups. The new guidelines allow for the surveillance of fewer patients.

Endoscopy units have been heavily affected by the Covid-19 pandemic, with European Society of Gastrointestinal Endoscopy (ESGE) and BSG guidance being to stop all but emergency and carefully vetted urgent cases. When restrictions begin to lift, measures to protect patients and staff will leave units operating far below their pre-pandemic capacity. The cancellation of so many procedures, together with reduced on-going operational volumes will lead to long backlogs of cases, and lengthy delays. The purpose of this prospective audit was to assess the impact of 're-triage' of all cases added to the colonoscopy surveillance list prior to the publication of the updated guidelines.

Aims & Methods: This was a prospective audit performed in a single London teaching hospital. All patients due to undergo surveillance endoscopy were identified using Cerner Electronic Health Records. All duplicate requests and requests for procedures other than colonoscopies were excluded. The updated BSG colonoscopy surveillance guidelines were then applied in a re-triage of all cases on the surveillance waiting list, with cases not meeting the updated criteria being cancelled (and an explanatory letter sent to the patient and their primary care doctor).

Results: There were a total of 1548 patients on the surveillance list, of whom 708 were re-triaged by clinicians involved in this audit. After exclusion of duplicates and non-colonoscopy endoscopies, there were 578 requests for surveillance colonoscopies. With application of the updated guidelines, 77.6% of the colonoscopies (448/578) were cancelled. With a tariff of £400 per colonoscopy this was a cost saving of £179,200, but equally importantly it freed up 75 full endoscopy lists (calculated at six colonoscopies per list) from surveillance cases no longer meeting national society guidance. Extrapolating this to the entire surveillance cohort gave figures of £391,810 saved and 163 endoscopy lists (or 979 individual procedures) created.

Conclusion: Re-triage of cases on the colonoscopy surveillance list, applying the latest BSG guideline criteria, resulted in around 80% of cases on the list being cancelled. This could be crucial in generating endoscopy capacity and helping meet the challenge of delays to performing endoscopy due to the current pandemic.

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Disclosure: Nothing to disclose

P1473

QUALITY OF LIFE IN PATIENTS WITH CIRRHOSIS DURING THE COVID 19 EMERGENCY: AN ITALIAN AWARENESS SURVEY

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Introduction: in December 2019, a novel coronavirus disease Covid 19 (C19) emerged in China, and quickly has become a global threat to human health. Its rapid spread has had a tremendous impact on the quality of life (QOL) of individuals, in particular of those with a chronic disease, including liver cirrhosis (LC) patients.

Aims & Methods: Our aim was to evaluate the awareness of patients with LC about the C19 emergency and how it impacted on their QOL. Patients with LC who had been evaluated at our outpatient Liver Disease clinic during the six-month period preceding the start of Italian lockdown (March, 9th, 2020) were enrolled. Lockdown was temporarily imposed by governmental authorities requiring that the population had to stay in their homes and refrain from/limit outdoor activities and public contact.

Participants were asked to complete a two-part questionnaire, administered by telephone according to governmental restrictions: first section assessed the basic knowledge regarding C19 infection, such as transmission, ability to recognize alarm symptoms, patients' awareness of being at an increased risk of developing more severe clinical form of this viral infection because of LC. Use of personal protective equipment (PPE), and how lockdown impacted contact with healthcare providers and their six months ultrasound follow-up program were investigated.

Second section evaluated the impact of the C19 emergency on the QOL of these patients, and we used the Italian version of the chronic liver disease questionnaire (CLDQ-I). To investigate and detect possible changes in QOL, this second section was administered by asking the patient to recall his/her quality of life perceptions at two different time points: "t0" two weeks before lockdown was imposed, and at a time "t1", two weeks before the date of enrollment.

All data were expressed as number (%), continuous variables reported as mean $\pm$ standard deviation (SD), and compared using the paired Student t-test.

Results: 83 consecutive patients were enrolled in the study 57 (68,7%) completed both sections of the questionnaire and were equally distributed by gender (51% males and 49 %females; mean age was 67,2 $\pm$ 11,3 yrs). Fifty-two (91,2%) had compensated cirrhosis (Child A5-A6). The majority (98,2%) were aware of C19 transmission modalities, and on how to recognize the most common alarm symptoms (95%), and to apply the correct use of PPE (93%).

Nine patients (16%) needed to contact their liver specialist, and 89% encountered difficulties in reaching them. Forty-nine (85,9%) were scheduled to undergo surveillance liver ultrasound aimed at early hepatocellular carcinoma detection during the lockdown time frame, and 40% (20/49) were not able to comply with this indication.

About the impact on QOL, most of the patients had negative mental health-related lifestyle changes with a worsening of anxiety ($p<0,0001$), and a more frequent sensation of irritability and depression ($p<0,0001$). Significant differences were also found in a worsening in sleeping ($p=0,0035$) and in falling asleep at night ($p=0,0007$). It was noticed an increase in the time spent thinking about a worsening of their condition ($p=0,0001$) and the possibility to never feel better again in the future ($p=0,0038$).

Conclusion: the C19 epidemic has had a significant impact on LC patients' QOL, despite their good knowledge of preventive measure and modalities of virus transmission. We describe a significant QOL worsening in patients with compensated liver cirrhosis, in whom impact of their chronic disease, although relevant, is nevertheless limited.

Disclosure: Nothing to disclose

P1474

HIGH PREVALENCE OF ISCHEMIC-LIKE GASTROINTESTINAL INJURY AMONG PATIENTS WITH SARS-COV-2 INFECTION: RESULTS FROM AN INTERNATIONAL MULTICENTRE ENDOSCOPY REGISTRY

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Introduction: Although Coronavirus Disease 2019 (COVID-19) primarily occurs as a respiratory disease, Gastrointestinal (GI) symptoms are frequent, SARS-CoV-2 receptor is highly expressed in the GI tract and viral RNA is frequently detected in stools, even when naso-pharyngeal swabs become negative. However, endoscopy findings have been scarcely reported.

Aims & Methods: This was a multicentre initiative to evaluate endoscopy findings in patients with SARS-CoV-2 infection and their correlation with patient- and hospitalization-related variables.

Endoscopies between February-May 2020 of 16 International centres in high-incidence areas were included. Findings were recorded using Standard Terminology by World Endoscopy Organization and synthesized in Acute-Major (A+), Acute-on-Chronic (AoC), Minor and Chronic abnormalities (Table1). ROC curves analyses were used to dichotomize continuous variables. Differences between A+ and Chronic/Minor/No (CMN) findings were explored, and significant variables tested by logistic regression.

Results: 114 endoscopies (87 upper and 27 lower) were included, 55.3% being urgent examinations for GI bleeding. Among patients, 71.9% were male, median age was 69 [59-75], ASA score was 3 in 50% and the most prevalent comorbidities were hypertension (52.3%) and diabetes (21.6%). 38 (33.3%) patients were admitted in Intensive Care Units. 41.8% reported GI symptoms, which consisted mainly of abdominal pain (26.5%) and diarrhea (14.3%).

A+ findings were found in 45.6%, while 11.4% bled from pre-existent conditions (AoC) and 43% had CMN

Compared with CMN patients, those with A+ findings were more frequently aged >73 (36.5% vs 18.4%, p=.04), with GI symptoms (53.1% vs 30%, p=.03), a D-Dimer above 1850 ng/ml (48.6% vs 22.6%, p=.03), a Platelet count below 317 x10⁹/L (48.6% vs 22.6%, p=.03) and without underlying atrial fibrillation (AF; 3.8% vs 16.7%, p=.04).

Using multivariate logistic regression, a D-Dimer level >1850 (OR=5.8 [1.1-31.4]), a platelet count <317 (OR=10.4 [1.2-89.1]) and any GI symptom (OR=7.5 [1.36-40.8]) were independently associated with A+ finding, while AF was associated with a lower risk (OR=0.07 [0.007-0.8]).

	Normal Examinations	Acute-Major findings		Minor findings		Chronic findings		Acute on Chronic findings	
Upper GI (N=87)	26/87 (29.9%)	Esophagitis	7/87 (8%)	Erythematous / Edematous Gastroduodenopathy	26/87 (29.9%)	Gastric Antral Vascular Ectasia	3/87 (3.5%)	Oozing esophageal varices	3/87 (3.4%)
		Petechial / Hemorrhagic Gastropathy	8/87 (9.2%)	Granular Gastropathy	2/87 (2.3%)	Atrophic Gastritis	3/87 (3.5%)	Oozing gastric polyp	2/87 (2.3%)
		Erosive / Ulcerative Gastroduodenopathy	13/87 (14.9%)	Esophageal Candidiasis	2/87 (2.3%)	Esophageal varices	5/87 (5.9%)	Oozing GAVE	2/87 (2.3%)
		Erosive / Ulcerative Jejunopty	1/87 (1.2%)			Angioectasia	1/87 (1.2%)		
		Gastroduodenal Ulcers	22/87 (26.4%)						
		Dieulafoy lesion	1/87 (1.1%)						
Lower GI (N=27)	5/27 (18.5%)	Ischemic-like Colopathy	9/27 (33.3%)	Unspecific Left Colon Erythema	2/27 (7.4%)	Segmental colitis associated with diverticulosis	3/27 (11.1%)	Ulcerative Inflammatory Colitis	1/27 (3.7%)
		Lower bleeding without other abnormalities	3/27 (11.1%)			Diverticulosis	4/27 (14.8%)	Bleeding Diverticulum	4/27 (14.8%)
						Hemorrhoids	1/27 (3.7%)	Bleeding Angioectasia	2/27 (7.4%)

[Endoscopy findings among SARS-CoV-2 patients]

Conclusion: Almost half of CoV-2 patients undergoing endoscopy have significant acute mucosal injuries, with a high prevalence of findings compatible with ischemic damage. Multivariate analysis of risk factors further endorse this pathogenetic hypothesis, in line with increasing evidence suggesting endothelial involvement and a “microvascular thromboinflammatory syndrome” as primer for COVID-19 districtual damage.

Disclosure: Nothing to disclose

P1475

ENDOSCOPIC ACTIVITY IN A TERTIARY CARE HOSPITAL DURING COVID 19 CRISIS

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Introduction: COVID-19 outbreak, caused by SARS-CoV-2, started in China in last December. The World Health Organization declared it as pandemic in March 2020. In Belgium, a Hospital Emergency Preparedness Plan and a global lockdown were announced 14th and 18th March, respectively. This included reorganization of all hospital departments and cancellation of endoscopic procedures which were not considered urgent or immediately necessary.

Aims & Methods: This study aims to assess the impact of this unprecedented health situation on the endoscopy unit of a tertiary care hospital. We reviewed, from a prospective database, all endoscopy procedures per-

formed from 16th March to 26th April 2020, and compared them to the activity of the same period during last two years (2018 and 2019). Procedures were classified as urgent (to be performed within 24 hours) or not. The activity was broken down by types of endoscopy (upper-GI (UGI), lower-GI (LGI), endoscopic ultrasonography (EUS) and endoscopic retrograde cholangiopancreatography (ERCP)). The proportion of procedures performed in positive COVID patients was also analyzed, as well as the impact of these measures on medical staff and material.

Results: During the lockdown, global GI endoscopy activity dropped by 74% (mean number of procedures 2018-2019: 1187, 2020: 306), with a more important decrease for non-urgent indications (-78% vs -51% for urgent; $p < 0.0001$). The decrease affected UGI, LGI, EUS and ERCP by 81%, 87%, 67% and 52%, respectively.

Major remaining indications for urgent procedures ($n=72$) were UGI and LGI bleeding (44% and 15%), biliary drainage (19%), treatment of fistula/collection drainage (6%), acute severe upper abdominal pain (6%), GI obstruction/foreign body extraction (4%) and others (6%). Urgent procedures were performed in COVID confirmed patients in 25% ($n=18/72$) of these cases.

Regarding activity decrease according to indications, endoscopies for LGI bleeding were more affected than those performed for UGI bleeding (-82% vs -29%). ERCPs performed for acute cholangitis dropped by 59% while those for newly diagnosed malignant obstructive jaundice were marginally affected (-7%)

Regarding resources, 21 of 38 (58%) physicians from the gastroenterology department, 7 of 29 (24%) nurses from the endoscopy unit, as 4/7 (57%) ventilators and 5/12 (42%) monitors were requisitioned for the COVID units. Five of our 12 endoscopic rooms were closed.

Conclusion: COVID-19 crisis caused a significant change in endoscopic activity with a decrease of diagnostic and low priority procedures. A number of therapeutic procedures (i.e. ERCP for cholangitis) may have decreased due to a more conservative, out-patient, initial medical management. The impact the above modifications may have on patients' health will be assessed in the coming months.

Disclosure: Nothing to disclose

P1476

CHALLENGES OF THE COVID-19 PANDEMIC IN GASTROINTESTINAL ENDOSCOPY: EXPECTATIONS AND IMPLEMENTATION OF RECOMMENDATIONS

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Introduction: The COVID-19 pandemic represents a major challenge for health care systems worldwide. Recent data suggests an increased risk for personnel of gastrointestinal (GI) endoscopy units due to a potential fecal infection route. Several societies have formulated recommendations for the current situation, but their feasibility is unclear and real-world data on preparedness of endoscopy units are lacking.

Aims & Methods: A web-based survey among German GI-endoscopy units was conducted from April 1st and April 7th, 2020. It comprised 33 questions based on the ESGE (European Society of Gastrointestinal Endoscopy) recommendations and was distributed electronically by the German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS).

Results: Of 551 completed surveys, 202 (37%) endoscopy units cancelled less than 40% of their procedures, whereas 196 (36%) cancelled more than 60%. Interestingly, small-volume (<4000 procedures in 2019) units cancelled significantly less procedures than high-volume (>4000) units (57% vs. 71% cancellation of >40% procedures, $p=0.004$). Complete spatial separation of patients with suspected or proven COVID-19 infection was possible in only 95 (17%) units. Most units systematically identified patients at risk (91%), used risk adapted personal protective equipment (PPE) (85%) and trained the personnel (89%). Larger units were better prepared in some aspects, as they consulted hygiene specialists (73% vs. 46%) and had a second team at their disposal more often (47% vs. 29%). For the future, shortages in PPE (83%), staff (69%) and relevant financial losses (80%) were expected.

Conclusion: Procedural measures were well adopted, but recommendations on structural and personnel conditions were only partially fulfilled and cancellations of procedures were heterogeneous. Concise definitions of non-urgent interventions are needed to better guide endoscopic activity. Special attention should be paid to expectations of GI-unit heads in order not to endanger further medical care.

Disclosure: Nothing to disclose

P1477

ACTIVITY AND SAFETY MEASURES IN THE ENDOSCOPY UNIT IN THE COVID19 ERA - A SINGLE CENTRE STUDY

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Introduction: As an aerosol-generating procedure, endoscopy is considered a high-risk activity. Based on the limited published experience, ESGE and many other organisations have issued recommendations regarding patient risk stratification, usage of personal protective equipment, and endoscopy procedure priority.

Aims & Methods: Bulgaria remains a low-risk area, since the reported incidence is currently 28,6/100 000 population (under 50/100 000 population). We have investigated the work in our endoscopy unit performed in the period of state of emergency in our country.

In this period, we have performed endoscopies with recommended high-risk protective equipment: FFP2 masks, gloves -two pairs, shoe covers, disposable hairnet, protective face shield, water-proof disposable gowns. In the period 13.03.2020-20.04.2020, we have performed only high-priority procedures.

After 20.04.2020, we have resumed some of the low-priority endoscopy procedures, only in case of COVID-19 PCR negative results from the last 24 hours. The personnel were PCR tested every two weeks.

Results: In the period 08.03.2020- 13.05.2020, 548 procedures were performed in our unit by three endoscopists and three endoscopy nurses. The distribution of procedures was as follows: 126 ERCP, 54 EUS, 238 gastroscopies, and 150 colonoscopies.

We have compared our activity with the previous year routine practice for the same period. As we are a referral centre for ERCP, the number of ERCP procedures has remained unchanged (120 for this period in 2019). The performed gastroscopies were 1.9 fold fewer (454 in 2019 and 238 in 2020) and the performed colonoscopies were 2.3 fold fewer (348 in 2019 and 150 in 2020) than those in 2019.

Among those who underwent an endoscopy procedure, there were two patients, positive for COVID-19. None of the personnel developed suspicious symptoms. The personnel members remain negative for COVID-19 as of 13.05.2020.

Bulgaria remains a low-risk area, since the reported incidence is currently 28,6/100 000 population (under 50/100 000 population). We have investigated the work in our endoscopy unit performed in the period of state of emergency in our country. In this period, we have performed endoscopies with recommended high-risk protective equipment: FFP2 masks, gloves -two pairs, shoe covers, disposable hairnet, protective face shield, water-proof disposable gowns. In the period 13.03.2020-20.04.2020, we have performed only high-priority procedures. After 20.04.2020, we have resumed some of the low-priority endoscopy procedures, only in case of COVID-19 PCR negative results from the last 24 hours. The personnel were PCR tested every two weeks.

Conclusion: We suggest that resuming the routine endoscopy work with high-risk protective equipment or with low-risk protective equipment plus patient PCR testing is safe for the personnel working at endoscopy units. The financial impact of these measures has not yet been investigated.

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Disclosure: Nothing to disclose

P1478 WITHDRAWN

P1479

FAECAL MICROBIOTA TRANSPLANTATION FOR *C. DIFFICILE* INFECTION DURING THE COVID-19 PANDEMIC: DESCRIPTION OF A SECURITY PROGRAM WITH HIGH-SUCCESS RATE

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Introduction: To face the pandemic of COVID-19, healthcare facilities have intensively decreased elective activities. Specifically, gastroenterological activities have been triaged according to risk and need. Faecal microbiota transplantation (FMT) is a life-saving procedure for patients with recurrent *C. difficile* infection (rCDI), and should be considered among the non-postponable gastroenterological procedures despite COVID-19.

Aims & Methods: Our aim is to describe the security measures applied to our FMT working protocol, and relative outcomes, during the COVID-19 pandemic.

Security measures applied to our colonoscopic FMT working protocol to prevent the transmission of SARS-CoV-2 included 1) application, whenever possible, of telemedicine to recruit donors, select and follow up patient; 2) multidisciplinary evaluation of patient with rCDI and COVID-19; 3) evaluation, in the donor questionnaire and in the patient triage, of: exposure to, known diagnosis of, or typical symptoms of, COVID-19; 4) nasopharyngeal swab and RT-PCR for SARS-CoV-2; 5) preference of frozen over fresh faeces, and use, until possible, of samples stored before January 2020; 6) use of full PPE during FMT, to be performed in a negative-pressure room; All patients treated with FMT for rCDI from March 8, 2020 to May 8, 2020 were enrolled. Demographic and clinical characteristics, as well as clinical outcomes (recurrence of CDI after treatment) were recorded. Follow-up visits were scheduled weekly (with video consultations when possible) up to 8 weeks after treatment.

Results: Overall, 15 patients received FMT for rCDI, during the study period (F=10; mean age 75). Five of them (33 %) were inpatients. All patients received at, a single fecal infusion, and three of them underwent two FMTs because of pseudomembranous colitis at baseline endoscopy, for a total of 18 procedures. One patient had underlying active ulcerative colitis, which ameliorate after a second FMT, and another patient was COVID positive, which CDI was refractory to fidaxomicin. At May, 15, 10 of 15 patients have completed the 8-week follow up, and no one recurred after FMT. In the remaining five patients follow-up is ongoing, although in all of them diarrhoea disappeared after the first procedure. No serious adverse events occurred, and no new COVID-19 infections were diagnosed.

Conclusion: Our preliminary results suggest that volumes, efficacy and safety of FMT for rCDI are not affected by the COVID-19 pandemic, if specific security measures are added to the working protocols of FMT centres. Dedicated guidelines to drive FMT protocols at the COVID-19 time are advocated.

Disclosure: Nothing to disclose

P1480

REDUCED RATE OF HOSPITAL ADMISSIONS FOR LIVER RELATED MORBIDITIES IN THE ERA OF COVID-19 PANDEMIC

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Introduction: Corona virus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has resulted in significant morbidity and mortalities worldwide. Complications of liver cirrhosis and acute hepatitis are major causes of liver related morbidities required hospital admissions.

Aims & Methods: This study aimed to investigate hospital admissions for liver related conditions during COVID-19 outbreak in a referral hepatology center. In a retrospective analysis, we recorded hospital admissions for liver related morbidities in a referral hepatology center in Pars province, Shiraz, Iran. The study period was considered the time between February 19 (the time of first confirmed patient with COVID-19 in the country) and April 30. Liver related conditions were defined as: acute hepatitis needing hospitalization as well as various complications of liver cirrhosis including gastrointestinal bleeding, spontaneous bacterial peritonitis (SBP), hepatorenal syndrome, hepatic encephalopathy and diuretic resistant ascites.

Hospitalization rates during the study period was compared to the corresponding time period in previous year (February 19 to April 30, 2019) as control time period. The outcome was the cumulative in hospital admissions for liver related complications needing hospitalizations. Incidence rates for the defined outcome were calculated by dividing cumulative number of hospital admissions by the number of days. Poisson regression was used for calculation of risk ratios comparing admissions during COVID-19 outbreak with the control time period.

Results: During February 19 and April 30 2020 (71 days), a total of 124 hospital admissions were recorded for liver related disorders. The mean age of patients hospitalized during the study period was 51.3 ± 16.4 years with 68 female patients (54.8 %) and 56 male patients (45.2 %). The causes of admissions during the study period was cirrhosis with gastrointestinal bleeding in 14 patients (12.2 %), SBP in 19 patients (15.3 %), hepatic encephalopathy in 19 patients (15.3 %), hepatorenal syndrome in 23 patients (18.5 %), diuretic resistant ascites in 7 patients (5.6 %), acute hepatitis in 6 patients (4.8 %) and complications of liver transplant recipients in 36 patients (29 %). The mean rate of hospital admissions for liver related complications during the study period was 1.74 admissions per day. There were 230 hospital admissions for liver related disorders during the control time in previous year (the mean rate was 3.23 per day). The rate of hospital admissions for liver related disorders during the study period was significantly lower compared to the control period in previous year (Incidence rate ratio: 1.85, 95% CI :1.49- 2.30; $P < 0.001$).

Conclusion: Our results demonstrate a significant decrease in total number of hospital admissions for liver related disorders during COVID-19 pandemic compared to the same months in previous year in a referral hepatobiliary center. The number of admissions for each cause of liver related complications were also decreased. Hepatologists will probably encounter cirrhotic and liver transplant patients with more drastic complications after the outbreak. COVID- 19 outbreak may have significant impact on quality care of patients with liver diseases.

Disclosure: Nothing to disclose

P1481

MENTAL STRESS OF MEDICAL STAFF DURING THE SARS-COV-2 PANDEMIC IN 2020 AND EFFECTS OF INTERPROFESSIONAL COLLABORATION ON QUALITY OF CRISIS MANAGEMENT

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Introduction: In times of crisis such as the SARS-CoV-2 pandemic, health care workers represent a valuable social resource. Health protection of each individual staff member must be essential. From previous health crises such as the outbreak of Ebola, SARS/MERS-coronaviruses we know that mental pressure and anxiety of physicians, nurses and other professional categories of the health care system play a critical role in coping with an acute crisis situation. They cannot only affect the health of health care professionals on long term, but also determine how fast the health care system can recover from such an extraordinary challenge. The world health organization (WHO) published guidelines concerning handling and reduction of stress to preserve mental health (WHO, Geneva, 2020)), pointing out interprofessional collaboration to be pivotal for the management

of stressful situations and the retention of psychologic resources. We hypothesized that by means of intensified interprofessional exchange the impact of psychosocial stressors on health care professionals would be impaired. Thus, this study investigated whether subjectively perceived interprofessional collaboration is in measurable context with mental health factors such as stress, anxiety or resilience.

Aims & Methods: This observational study consists of four different, but complementary lines of questioning based on an extensive questionnaire. The study included staff with different health care professionals (physicians and nurses as well as volunteer workers, such as medical students, from diverse fields (intensive care, internal medicine, anesthesia, virology), working in variable extent of interprofessional collaboration. Some of the teams intensified interprofessional communication by means of shared morning briefings, instructions and implementation of interprofessional working routines.

The questionnaire assessed demographic data such as gender, age group, marital status and workload, aiming at identifying primary groups at risk. Based on pandemic specific stressors (Petzold et al. 2020), in depth questioning determined the main stressors within the study population. PHQ-9 and GAD-7 questionnaires screened for suspected depression and generalized anxiety disorder. Fears directly associated with SARS-CoV-2 were also assessed.

Finally, the questionnaire focused on interprofessional collaboration experienced in everyday working routine. Analyses were performed using IBM SPSSR software.

Results: A total of N=293 healthcare professionals (22 physicians, 159 nurses, 112 others) completed the questionnaires (response rate 47%). This sample is part of an ongoing study and represents interim results. Considering professional categories, gender and direct contact to patients infected with SARS-CoV-2 we present the following findings: Perception of both, poor interprofessional communication and insufficient crisis management, is associated with higher pressure caused by the pandemic, depression and anxiety. The worse interprofessional collaboration within the team was evaluated, the higher were pressure score and anxiety caused by SARS-CoV-2.

Conclusion: These results highlight the importance of intensified interprofessional collaboration for medical health care workers, improving coping mechanisms and contributing to alleviating stress and pressure caused by working under the state of emergency. Our findings thus contribute to improve psycho-protective tasks in clinical health care during the ongoing SARS-CoV-2 pandemic and enforce the importance of developing preventive concepts for future challenges.

Disclosure: Nothing to disclose

P1482

INFLAMMATORY BOWEL DISEASE AND SARS-COV-2 PANDEMIC - THE PATIENT'S PERSPECTIVE

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Introduction: Since the onset of Covid-19 pandemic concerns regarding the management of IBD patients has emerged. Although there is no evidence so far that IBD patients are more susceptible for the virus and there is currently no evidence for aggravated outcomes, patient education on preventive tasks has never been so important.

Aims & Methods: We conducted a questionnaire survey to evaluate the patients' attitudes to infectious diseases in general and Covid-19 particular. A 58-question anonymous web-survey was conducted between 22 March and 3 April 2020 for adult IBD patients. Topic specific questions included relation to infectious diseases, sources and credibility of information, and fears regarding SARS-CoV2 virus, changes in medical and social activities. Continuous variables were evaluated on a five-point scale.

Results: Responses were classified according to patients' gender, age, disease duration, education, class of medication used, and disease activity. Average anxiety level was higher regarding Covid-19 compared infections in general (3.4 ± 1.2 vs. 2.8 ± 1.1 , $p < 0.05$). Female gender, older age lower educational level, immunomodulatory and biologic therapy had a statistically significant negative impact on this. Same groups used personal protective equipment more frequently and maintained social protection measures. 93% of patients gained information from internet, 35% visited portals of patients association (PPA) and 16% interviewed a gastroenterologist. Data from the PPA and the gastroenterologist were evaluated as the most reliable. Minority of patients changed their medications.

Conclusion: Covid-19 pandemic revealed high level of anxiety among IBD patients in Hungary. Most vulnerable patients are female, older and lower educated patients and patients on immunosuppressants or biologic therapy. Patient associations' portals are the most reliable and at the same time the most widely available source of authentic information. Patients made little change in their treatment.

Disclosure: Nothing to disclose

Poster presentations
Health economics / Digitalisation in GI
Education In GI / Gender and diversity

Poster Presentations

Health economics / Digitalisation in GI / Education In GI / Gender and diversity

Health economics / Digitalisation in GI / Education In GI / Gender and diversity

09:00-19:00 / Poster Exhibition

P1483

A COST-UTILITY ANALYSIS COMPARING THE TOTAL COST OF REUSABLE DUODENOSCOPES TO SINGLE-USE DUODENOSCOPES

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Introduction: In the USA more than 500,000 endoscopic retrograde cholangiopancreatographies (ERCPs) are performed annually. Multiple studies have shown that contaminated duodenoscopes can lead to infection with multi-drug resistant organisms (MDROs). This will likely cause a decrease in the patients' quality of life (QoL) and may lead to additional healthcare cost. Currently, ERCP procedures is most often performed using reusable duodenoscopes; nevertheless, cleaning of reusable duodenoscopes is difficult due to complex design compositions, and single-use equipment have been proposed as an alternative and safer technology for ERCPs.

Aims & Methods: The aim of this study was to investigate the expected incremental costs and consequences of reusable versus single-use duodenoscopes. A decision analytic (Markov) model was designed in TreeAge Pro with the following stages; *no infection*, *infection*, *post infection*, and *dead*. A 10-year cycle was applied based on the assumption that either all patients are healthy or dead within the time horizon. Two systematic literature reviews were conducted in PubMed and Embase from January 2010 to March 2020, to identify studies assessing quality-adjusted life years (QALYs), contamination, and infection data. QALY data included a baseline and a 12-months follow-up. Contamination data were based on the rate of contaminated duodenoscopes (positive samples) and infection data contained number of duodenoscope-related infections following ERCP.

The endoscope-related infection risk was calculated using R Studio® and the *metafor* package using a random effects model. Cost data were collected from seven US endoscopy units using micro-costing method. Capital cost were annuitized using a 3.5% discount rate (6).

All costs are presented as 2019 prices in USD. The cost for using a reusable duodenoscope was calculated as a weighted average based on procedure volume. The cost of treating an MDROs was obtained from HCUPnet using relevant ICD-10 codes.

Results: Base-case results illustrate an additional cost of \$38,591 per QALY. Thus, the single-use duodenoscope is cost-effective at a willingness-to-pay (WTP) at \$50,000-\$150,000 per QALY using an estimated cost at \$1,500 per single-use duodenoscope. The endoscope-related infection risk was estimated at 1.11% based on available literature. The endoscope-related infection risk was used as the transition probability between no infection and infection in the Markov model.

The weighted per-procedure cost for a reusable duodenoscope was \$423 (range: \$239 - \$3,659) and the cost for treatment of an infection with MDRO is \$47,181. For single-use duodenoscope a 0% endoscope-related infec-

tion risk was assumed. The QoL from the literature review are stated as 0.8810 for no infection, 0.275 for infection, 0.639 for post-infection, and 0 for dead.

Conclusion: We found that single-use duodenoscopes are cost-effective at a WTP \$50,000-\$150,000 per QALY. To support and validate the findings of this study more evidence is needed to confirm the endoscope-related infection risk and the subsequent effects on the patients' QoL.

Disclosure: Sara Larsen and Rasmus Vinther Russell are both employed by Ambu A/S, Ballerup, Denmark

P1484

THE IMPACT AND IMPLICATIONS OF THE COVID-19 PANDEMIC ON THE ACTIVITY OF THE ENDOSCOPY DEPARTMENT OF A TERTIARY REFERRAL CENTER

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Introduction: The COVID-19 pandemic is an unprecedented global medical emergency, causing an unforeseen tremendous burden on healthcare resources worldwide. National and international gastrointestinal societies have strictly recommended that any endoscopic activity during the pandemic should be limited to emergency or non-deferrable procedures only.

Aims & Methods: To assess the impact of these mitigating measures applied during the COVID-19 pandemic on a busy tertiary referral endoscopy unit in London in terms of endoscopy activity, potential missed cancers and financial implications. We also aimed evaluate the resultant effect of these measures based on their potential duration through projected, arbitrary cut-offs of a total of 5, 6 or 7 weeks, respectively.

The number of the endoscopy procedures cancelled and performed in our endoscopy unit during our 'delay phase' (16-22/03/2020) and 'lockdown phase' (23/03-03/04/2020) was reviewed and compared with endoscopy activity conducted during the same 3 weeks in 2019. The financial impact was subsequently analysed. A projection of the impact on endoscopy activity caused by a potentially prolonged lockdown of 5, 6 and 7 weeks, respectively was estimated as well as the potential number of missed cancers. Statistical examination was performed using Stata 16™ (StataCorp 2019, Stata Statistical Software: Release 16. College Station, StataCorp LLC, TX, USA). The financial implications of these cancellations on our endoscopic unit were estimated with reference to the 2019/2020 National Tariff Payment System, which is an official set of coded tariffs, established by the United Kingdom's National Health Service for care providers and commissioners.

Results: Between 16/03/2020 and 03/04/2020 a total of 479 procedures were cancelled and 130 non-deferrable procedures were performed. In contrast, in 2019, 640 procedures were performed over the same time-frame, resulting in a revenue contraction of approximately £364,579. We estimated a potential backlog of 665-931 endoscopic procedures ac-

cumulated over a period of 5-7 weeks of lockdown, requiring between 136-226 endoscopy lists after the 'lockdown phase', considering any potential delays to lists caused by safety precautionary measures. Regarding the potential missed cancers, nine cancers were newly diagnosed from 23/03/2020 and 03/04/2020. This yielded a 55.6% (confidence intervals (CI) 21.2-86.3%) decrease in the rate of cancer diagnosis. The projected number of potential missed cancers during lockdown would therefore be 11 (CI 4-17), 14 (CI 5-22) and 17 (CI 7-26) for the optimistic, realistic and pessimistic scenarios, respectively.

Conclusion: The results of our study highlight that even during the first 3 weeks of these essential restrictive measures; the COVID-19 pandemic has already had a considerable negative clinical and economic impact on our endoscopy service provision. Furthermore, analysis of our projected figures shows that the impact of the COVID-19 pandemic may have even more severe repercussions on future hospital activity and economics, as we aim to recuperate any cancelled or postponed activity. In addition, the potential, wide-ranging repercussions of delay in cancer care and other pathology is still not fully understood and studies to shed further light on this are required.

Disclosure: Alberto Murino has acted as a consultant for Boston Scientific and GI supply. He has also received academic grants from Fujifilm, Aquilant Endoscopy, Norgine and Olympus. Edward J. Despott has acted as a consultant for Boston Scientific and Ambu. He has also received academic grants and speaker honoraria from Fujifilm, Aquilant Endoscopy, Norgine and Olympus. The other authors have declared no potential conflict of interest.

P1485

RESOURCE UTILIZATION AND COSTS ASSOCIATED WITH INTRAVENOUS IRON INFUSIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND IRON DEFICIENCY ANEMIA OR HYPOFERRITINEMIA: REAL-WORLD EVIDENCE FROM THE UK

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Introduction: Iron deficiency anemia (IDA) is a common outcome of inflammatory bowel disease (IBD), arising from the combined effects of gastrointestinal blood loss and reduced iron absorption. Intravenous (IV) iron is the preferred treatment option in patients with severe anaemia or in patients refractory/intolerant to treatment with oral iron. Two high-dose, rapid-infusion IV iron formulations are currently available in the UK: iron isomaltoside 1000/ferric derisomaltose (FDI) and ferric carboxymaltose (FCM), differing in the nature of the carbohydrate with which the iron is complexed and the approved posology; FDI can be dosed up to 20 mg/kg bodyweight, while FCM can be dosed up to a maximum of 1,000 mg.

Aims & Methods: The aim of the study was to evaluate the resource utilization and cost associated with treating IDA or hypoferritinemia with FDI versus FCM in patients with IBD in the United Kingdom (UK).

Data from 91 patients with IBD and either IDA or hypoferritinemia having received IV iron treatment at two UK gastroenterology services were pooled and analyzed using the R statistical programming language. Of the included patients, 28 received FDI and 63 received FCM. Baseline age, bodyweight, hemoglobin, ferritin, and calculated iron need were compared between the FDI and FCM treatment groups, and the total number

of infusions administered to replenish the iron requirement was calculated. The average cost of treatment was then modeled using two approaches: healthcare resource group (HRG) tariffs from the UK Department of Health (DoH) perspective and a microcosting analysis from an NHS Trust perspective. The HRG tariff approach utilized a weighted cost based on the 2019-20 tariff values for day cases and ordinary elective spells weighted by the combined day case and elective spell activity from 2018-19. The microcosting analysis captured observation and infusion time based on data from the summaries of product characteristics (SPCs) and the Personal Social Services Research Unit (PSSRU), costs of IV iron from the British National Formulary, and costs of giving sets, cannulas, and dressings from the NHS Business Services Authority and NHS Supply Chain.

Results: None of the recorded baseline characteristics significantly differed between the FDI and FCM treatment groups ($p > 0.05$ for baseline hemoglobin, ferritin, and bodyweight). Patients treated with FDI received an average of 1.14 infusions to address the iron requirement (32 infusions in 28 patients), compared with 1.56 infusions with FCM (98 infusions in 63 patients). The economic analysis based on HRG tariffs showed that this would result in savings of GBP 121 per patient (GBP 334 with FDI versus GBP 455 with FCM), while the micro-costed analysis showed cost savings of GBP 23 per patient (GBP 220 with FDI versus GBP 243 with FCM) from the NHS Trust perspective.

Conclusion: An analysis of real-world data from two gastroenterology services in the UK showed that using FDI in place of FCM would result in 0.42 fewer infusions per patient to treat either IDA or hypoferritinemia in patients with IBD. In the UK, this reduction would be associated with cost savings of GBP 121 per patient from the national DoH perspective or savings of GBP 23 per patient from an NHS Trust perspective. The reduction in infusions associated with FDI also has the potential to free up infusion suite capacity for other patients, or other IV infusions in the same patient group.

Disclosure: KDK, FM, MJ and AD have no conflicts of interest to declare. RP is a director and shareholder in Covalence Research Ltd, which received consultancy fees to conduct the analysis and draft the abstract from Pharmacosmos UK Ltd, a subsidiary of Pharmacosmos A/S, the marketing authorization holder for ferric derisomaltose.

P1486

ECONOMIC MODELS USED TO EVALUATE THE COST-EFFECTIVENESS OF BIOLOGIC TREATMENTS FOR ULCERATIVE COLITIS: A SYSTEMATIC LITERATURE REVIEW

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Introduction: Ulcerative colitis (UC) is an inflammatory bowel disease characterized by episodic or chronic inflammation of the colonic mucosa resulting in diarrhoea, rectal bleeding and reduced quality of life. The number of treatments for moderate-to-severe UC in Europe has increased with the introduction of biologic therapies such as tumour necrosis factor (TNF) inhibitors (e.g. infliximab, adalimumab) and targeted therapies (e.g. vedolizumab, golimumab). As such, economic evaluations are critical for informing clinical practice and in the reimbursement decisions for these treatments.

Aims & Methods: The aim of this systematic literature review (SLR) was to identify economic analysis publications, conference abstracts and health technology assessments for biologic therapies in adults with moderate-to-severe UC in Europe. Literature searches were carried out in MEDLINE,

Embase, EconLit and the Cochrane Library for articles published between 1 January 2012 and 22 June 2018. Conference proceedings were limited to those published between 1 January 2015 and 2 August 2018. Bibliographic lists of relevant SLRs were also interrogated. Study selection was guided by pre-specified inclusion and exclusion criteria.

Results: Thirteen economic evaluation publications were identified that included 15 economic models. In two studies, a societal perspective was considered. Biologics studied were adalimumab, golimumab, infliximab, infliximab biosimilars and vedolizumab. Six studies carried out from 2013 to 2016 included surgery as a comparator whereas studies carried out after 2016 did not. Nine studies included conventional therapy (e.g. corticosteroids, mercaptopurine, azathioprine) and two included cyclosporine as a comparator. Only one study evaluated sequencing of biologic therapies. Economic models used were Markov models ($n = 8$), a hybrid decision tree-Markov model ($n = 6$) and, in one case, a cost calculator alongside a clinical trial. The time horizon of analyses ranged from 1 year to lifetime. Key health states assessed were remission, mild disease, moderate and/or severe disease, surgery and death. All but one of the 15 models included health states associated with surgical outcomes. All studies considered the anti-TNF-naïve population; whereas two studies also evaluated the value of vedolizumab in anti-TNF-failure populations.

Conclusion: In this literature review, several model structures for the economic evaluation of UC were identified alongside various time horizons. As more treatment options have become available, surgery, although considered curative, has transformed from a treatment comparator to a health state. Future economic evaluations may need to consider the impact of sequencing of biologics, which may result in a shift towards longer time horizons and more hybrid decision tree-Markov models.

Disclosure: This study was funded by Shire Human Genetic Therapies, Inc., a Takeda company. Arpita Nag is an employee of Shire, a Takeda company. Molly Purser, Louise Hartley, Stephanie Earnshaw and Rikal Bhaila are employees of RTI Health Solutions, an independent research organization, which received funding from Shire, a Takeda company, for this and other studies and from other pharmaceutical companies that market drugs for the treatment of patients with Crohn's disease and other medical conditions. Medical writing support was provided by Maxine Cox of PharmaGenesis London, London, UK, and was funded by Shire International GmbH, a Takeda company.

P1487

SYSTEMATIC LITERATURE REVIEW TO ASSESS THE HEALTHCARE RESOURCE USE AND COSTS ASSOCIATED WITH ULCERATIVE COLITIS IN ADULTS IN EUROPE

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Introduction: Ulcerative colitis (UC) is an inflammatory bowel disease characterized by periods of episodic or chronic inflammation of the colonic mucosa. New biologic treatments for moderate-to-severe UC are becoming increasingly available. As such, there is a need to understand healthcare resource utilization (HCRU) in UC and the costs associated with its treatment.

Aims & Methods: The aim of this systematic literature review (SLR) was to identify HCRU and direct and indirect (out-of-pocket costs and patient and caregiver productivity losses) cost publications in adults with UC in Europe. Literature searches were carried out in MEDLINE, Embase, EconLit and the Cochrane Library for articles published between 1 January 2012

and 22 June 2018. Conference proceedings were limited to those published between 1 January 2015 and 2 August 2018. Bibliographic lists of relevant SLRs were also interrogated. Study selection was guided by pre-specified inclusion and exclusion criteria.

Results: Thirty-seven publications were identified: 34 reported HCRU and/or direct costs and 15 reported productivity and/or indirect costs. Various methodologies including prospective questionnaires, claims analyses, observational studies, surveys and randomized controlled trials were used to identify HCRU in UC. The most frequently reported resources used were related to hospitalization ($n = 24$ studies) and medication use ($n = 22$ studies), followed by surgery ($n = 15$ studies). Total annual direct costs ranged from €1230 per person in a country where biologics are under-utilized to €104 546 per person in patients with moderate-to-severe active disease who had just initiated a biologic.

The rate of hospitalization ranged from 0% in patients with stable remission to 42.7% in patients who were hospitalized for ≤ 1 day, with two studies reporting high rates in patients with more severe UC compared with patients with less severe UC. In one study, hospitalization (23%) and surgery ($< 1\%$) accounted for less of the total healthcare costs than biologic therapies (31%, rising over 2 years to 39%).

In another study, the authors reported that since the introduction of infliximab, hospital costs for patients with UC have decreased. Annual indirect costs ranged from €185 per patient to €13 719 in patients with active disease.

Conclusion: Although populations and parameters differed between studies, making it difficult to generate comparisons, the treatment of UC was found to result in a major economic and patient burden. Since the introduction of biologics for treating moderate-to-severe UC, rates of surgery and hospitalization have decreased, leading to a reduction in the cost of these resources. However, with the introduction of biologics, the cost drivers in patients with UC have switched from the cost of hospitalization and surgery to the cost of the medication.

Disclosure: This study was funded by Shire Human Genetic Therapies, Inc., a Takeda company. Arpita Nag is an employee of Shire, a Takeda company. Molly Purser, Louise Hartley, Stephanie Earnshaw and Rikal Bhaila are employees of RTI Health Solutions, an independent research organization, which received research funding from Shire, a Takeda company, for this and other studies and from other pharmaceutical companies that market drugs for the treatment of patients with Crohn's disease and other medical conditions. Medical writing support was provided by Maxine Cox of PharmaGenesis London, London, UK, and was funded by Shire International GmbH, a Takeda company.

P1488

COMPARE AND CONSULT: THE BURDEN OF INPATIENT CONSULTATION IN DIFFERING HOSPITAL SYSTEMS

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Introduction: The workload on Gastroenterology services continues to increase. While providing an inpatient general medical service, outpatient specialty service and diagnostic and interventional endoscopy, there is also a significant burden of inpatient consultation. The degree of this consultation burden can vary depending on both institution-specific and Departmental factors including but not limited to hospital size, nature of other specialties and Departmental staffing levels.

Aims & Methods: To quantify the nature, source and amount of GI consultation requests in a 600 bed Model 4, academic, tertiary referral Centre and perform a comparison with a 340 bed Model 3, University Centre.

The online consultation request system in the Model 4 hospital was used to analyse the number and nature of consultation requests over the previous 9 months. A comparison was then compared to data from the Model 3 institution over the previous year to evaluate differences in total burden, consultation source and nature of consultation request as well as appropriateness of the consult based on the Hounslow Clinical Commissioning Group Referral Guidance 2013. SPSS was used for statistical analysis.

Results: During the timeframe 154 referrals were made in the Model 4 Hospital from 22 specialties, while 174 were made in the Model 3 Hospital from 8 specialties. There was a higher rate of referral in the Model 3 hospital when adjusted for time and hospital size. There was no significant difference in the proportion of consults from general surgical specialties (31.8% vs 39.7% $p=0.23$) however, referrals from medical specialties were significantly more common in the Model 3 centre (42.4% vs 56.3% $p=0.04$). There were significantly more consultation requests for colitis seen on CT (16.9% vs 29.4% $p=0.04$) and liver disease (0% vs 26.4% $p<0.05$) in the Model 3 centre, while there were significantly more referrals for diarrhoea (14.9% vs 2.8%, $p<0.05$) in the Model 4 hospital. All consults in both centres were considered to be in an appropriate category.

Conclusion: There is a significant burden of inpatient consult requests on Gastroenterology Departments in both Model 3 and Model 4 Centres. While, as expected, the source of consults is more varied in a Model 4 centre due to more specialties in place, there was a higher per patient rate of referral in the Model 3 centre. There was a similar proportion of referrals from surgical specialties in both centres.

Disclosure: Nothing to disclose

P1489

COST EFFECTIVENESS OF NALDEMEDINE USED FOR OPIOID-INDUCED CONSTIPATION IN ACCORDANCE WITH UEG CONSENSUS IN THE UK

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Introduction: Opioid-induced constipation (OIC) is the most common adverse effect reported in patients receiving opioids to manage pain. Initial treatment with laxatives provides inadequate response in some patients and are generally poorly tolerated. The 2019 UEG European expert consensus statement (1) recommends the use of peripherally acting μ -opioid receptor antagonists (PAMORAs) in primary care among laxative refractory patients who have either OIC or mixed aetiology constipation with an OIC component. Naldemedine is a PAMORA used to treat patients with OIC who have previously received a laxative.

The objective of this study was to evaluate the cost-effectiveness of naldemedine when used within its marketing authorisation and in accordance with UEG expert consensus in the UK National Health Service (NHS).

Aims & Methods: A cost-utility model was constructed in Microsoft Excel to compare not only oral naldemedine 200 micrograms daily+standard-of-care (NLD+SOC) with placebo (PLB)+SOC in non-cancer patients receiving opioids for chronic pain (base case) but also scenarios comparing of NLD versus other comparators in patient subgroups with either non-cancer chronic pain or cancer pain.

The model comprised a decision tree for the first 4 weeks of treatment followed by a Markov model with a 4-week cycle length and four health states: 'OIC', 'non-OIC (treated)', 'non-OIC (untreated)' and 'death'. The

52-week COMPOSE-3 (C3) randomised placebo-controlled trial intention-to-treat population (2) provided base case inputs on efficacy, health state transition probabilities, and adverse event frequency; other COMPOSE trial data (3,4) informed scenario analyses. Active treatment comparisons were made by published network meta-analysis (5). Treatment-specific health state utilities (reflecting quality of life (QOL)) were derived from either published sources (6) or mapped (7) from PAC-QOL trial observations. Resource utilisation data were sourced from analysis of electronic medical records of routine clinical practice in the UK. The NHS payer perspective was adopted; costs and benefits were discounted equally at 3.5% per annum. The model time horizon was 5 years, reflecting the 90th centile of prescribed opioid analgesic duration observed in primary care. Model validation was conducted by not only an expert advisory group but also by the Evidence Review Group for the National Institute of Health and Care Excellence and economic assessors for the Scottish Medicines Consortium.

Results: NLD+SOC has an incremental cost-effectiveness ratio (ICER) of £12,489 per quality-adjusted life-year (QALY) gained versus PLB+SOC in non-cancer chronic pain, and £9,059 per QALY gained versus PLB in cancer pain (2019 values). The ICER remains stable whether NLD is used either as monotherapy+rescue laxative (£12,556; C1&2 pooled ITT) or in combination with laxative (£9,462; C3 stable laxative subgroup) versus PLB. NLD was dominant over naloxegol, assuming discontinuation parity, in non-cancer chronic pain patients and dominant over subcutaneous methylnaltrexone in patients with cancer pain.

Model outcomes were only sensitive to variations in utility inputs. Probabilistic sensitivity analyses for the base case indicate that NLD+SOC has an 86% probability of being cost effective at a £20,000 willingness-to-pay threshold when compared with placebo+SOC.

Conclusion: Naldemedine is highly likely to be a cost-effective treatment option for patients with OIC who have previously received a laxative when used in accordance with European expert guidance regardless of the clinical setting.

Disclosure: This abstract is funded by Shionogi BV and Peter Conway is an employee of Shionogi BV

P1490

IMPACT ON HEALTHCARE RESOURCES OF SWITCH FROM FAECAL OCCULT BLOOD TEST TO FAECAL IMMUNOCHEMICAL TEST WITHIN THE UK BOWEL CANCER SCREENING PROGRAMME - A SINGLE SCREENING CENTRE STUDY

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Introduction: From July 2019, Faecal Immunochemical Test (FIT) replaced Faecal Occult Blood Test (FOBT) in England as the Bowel Cancer Screening Programme (BCSP) screening tool for individuals aged 60 to 75. FIT was introduced in England at a starting sensitivity threshold of 120ug/g. Although some effect upon services were expected after a pilot testing noted increased screening uptake from 59.3% to 66.4%¹ and the theoretical advantage of FIT to detect human haemoglobin in stool, the extent of the changes upon service demand has not been assessed in the full UK national BCSP.

Aims & Methods: We aimed to assess the impact of the switch over from FOB to FIT on BCSP associated resources at our bowel cancer screening programme centre. Data from all patients booked for appointments with a Specialist Screening Practitioner (SSP) after either a positive FOBT (from December 2018 to May 2019) or FIT (from September 2019 to February

2020) test from our screening hub was analysed. The period between June 2019 and August 2019 was excluded due to a cross over period between the 2 kits. Endoscopy, radiology and surgical procedures as well as histology and SSP time were recorded. 45 minute slots of SSP time were allocated for each of the initial consultations, attendance at colonoscopy and colorectal multidisciplinary team meeting (if applicable); 20 minute slots for attendance at flexible sigmoidoscopy and EMR consent appointment. Subsequent follow up telephone or clinic consultations were allocated 10 minutes. Statistical testing was undertaken with an unpaired t-test. Endoscopy procedures took place at one of 3 endoscopy units across the area covered by our centre.

Results: In the FOBt group, 400 patients attended appointments after a positive test. An increase of 54% (n=216) in patients was observed, with a total of 616 patients attending in the FIT group (224 male in FOBt vs. 365 in FIT, p=0.30).

Comparing the 6 month periods, the FIT positive cohort required 284 more endoscopic procedures (608 vs. 371 colonoscopies and 100 vs. 53 flexible sigmoidoscopies). There were 436 hours of additional SSP time required and a 97% increase in the endoscopic polyp/biopsy samples with 538 extra specimens. There were more polyps found within the FIT group (n=974 vs. 466). This resulted from both a increase in the proportion of patients with polyps in the FIT group (53.3% vs. 46.5%, p=0.034) as well as a greater mean number of polyps per patient with polyps in the FIT group (2.97 vs. 2.49, p=0.0237). The total numbers of radiological investigations were also increased by 40% (117 in FIT vs. 83 in FOBt, p=0.51). Patients with malignancy requiring surgery (44 vs. 25) or palliative oncological treatment (3 vs. 2) were higher in the FIT group thereby almost doubling surgery and oncology resources needed. Estimation of financial impact is underway.

Conclusion: The change to FIT testing within our service has led to notable increases in service demand on SSP time, endoscopy procedures and histopathology services. Main contributing factors appear to be the higher numbers of patients presenting with a positive FIT along with the high numbers of polyps found within the FIT tested patients. Analysis of this impact aids workforce and service planning in NHS sites delivering BCS.

References: Moss S, Mathews C, Day TJ et al. Increased Uptake and Improved Outcomes of Bowel Cancer Screening With a Faecal Immunochemical Test: Results From a Pilot Study Within the National Screening Programme in England. *Gut*, 66 (9), 1631-1644 Sep 2017.

Disclosure: Nothing to disclose

P1491

EVALUATION OF QUALITY FOR MOBILE HEALTH APPS FOR GASTROINTESTINAL DISEASES

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Introduction: Digital transformation and mobile health are significant issues in current health care. A widespread bundle of mobile health care applications (MHA) is available for gastrointestinal disorders via APP-stores. For the user the quality, dangers and potential impact of the APPs remain often unclear. This systematic review aimed to evaluate the quality, characteristics as well as privacy, and security measures of MHAs for gastrointestinal diseases in the European commercial app stores.

Aims & Methods: In the European Apple APP- and Google Playstore, a web-crawler systematically searched for MHA for gastrointestinal diseases. The identified MA were evaluated using the *Mobile Application Rating Scale (MARS)*, assessing the subscales user engagement, functionality, aesthetics, and information quality. Furthermore, app characteristics such as price, affiliation, data safety and methods of information transfer were collected.

Results: 278 MHA were included. Content included e.g. education, advice, monitoring and measurements of gastrointestinal illnesses. The overall quality of the MHA was moderate 3.32(±0.67) (mean±SD) whereas mean star rating was 3.98(±0.86). Most apps (n = 248, 89%) were free of charge. Only 6 MHA were developed according to gastroenterological guidelines. n=224 (81%) focused on educational information about gastrointestinal diseases. Over half of the apps (n=188, 68%) offered specific advice. Security of data transfer was guaranteed only by n=40 (14%).

Conclusion: Objective analysis using rating scales as MARS offer the opportunity to identify MHA with positive impact on diagnosis, therapy and patient guidance in gastroenterology. Major concerns remain regarding data security and proof of efficacy in current range of mobile health care applications.

Disclosure: Nothing to disclose

P1492

SHARED CLINICAL MANAGEMENT IN GASTROINTESTINAL DISEASES: MOTIVATION AND UTILITY OF E-CONSULTATION

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Introduction: Shared management strategies in gastrointestinal diseases between general practitioners (GPs) and gastroenterologists based on e-consultation, open access endoscopy units and common clinical protocols can increase the efficiency on diagnosis and therapeutics processes. However, the information on e-consultation motivation and utility is still limited.

Aims & Methods: The aim of this study is to analyze the reasons to perform e-consultation from primary healthcare, the recommendations made by gastroenterologists and the effect of these recommendations. We designed an observational and descriptive study in Ourense, north-western Spain. We evaluated the e-consultations performed during January 2019. We recorded the demographic variables of the patient, the motivation for the e-consultation (diagnosis, management and/or revision), the recommendations made by the gastroenterologist (diagnosis, management and/or revision/derivation), and the effect of the different recommendations (laboratory test, endoscopy, image test and/or treatment changes).

Results: 270 consultation were analyzed (3,7% lost). Mean age was 59 years old (SD 1.2) and 54.5% were female. E-consultation were requested for diagnosis evaluation in 72.1% of cases, management strategies in 19.7% and to evaluate revision in 21.3%. The gastroenterologist made a diagnostic recommendation in 68.4% of patients, a treatment evaluation

in 20.5% and a derivation or revision suggestion in 41.4%. A laboratory test recommendation was made in 17.6% of cases (81.4% completed), an endoscopy in 29.5% (81.9% completed), an image test in 9% (86.4% completed) and treatment modification in 13.5% (48.5% completed).

Conclusion: Most of e-consultation made by GPs are related to diagnosis process and several consultation reasons are included. Gastroenterologists recommendations related to complementary tests are usually performed although the implementation of treatment recommendations is lower.

Disclosure: Nothing to disclose

P1493

DIFFERENTIATION BETWEEN MALIGNANT AND BENIGN ENDOSCOPIC IMAGES OF GASTRIC ULCERS USING DEEP LEARNING

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Introduction: Endoscopic differentiation between malignant and benign gastric ulcers (GU) affects further evaluation and prognosis.

Aims & Methods: The aim of our study was to develop and evaluate a deep learning algorithm for discrimination between benign and malignant GU in large database of endoscopic ulcers images.

Methods: We retrospectively collected consecutive upper gastrointestinal endoscopy images of GU performed between 2011-2019 at the Sheba Medical Center. All ulcers had a corresponding histopathology result of either benign peptic ulcer or gastric adenocarcinoma.

A convolutional neural network (CNN) was trained to classify the images into either benign or malignant. Endoscopies from 2011-2016 were used for training and from 2017-2019 were used for validation.

Results: Overall, our dataset included 1978 GU images; 1894 images from benign GU and 84 images of malignant ulcers.

The CNN showed an AUC of 0.89 (95% CI 0.836 - 0.940) for detecting malignant ulcers. For Youden's index, the network showed a sensitivity 82% of and specificity of 82% for malignant ulcers.

Conclusion: Our study displays the applicability of a CNN model for automated evaluation of gastric ulcers images for malignant potential. Following further validation, the algorithm may improve accuracy of differentiating benign from malignant ulcers during endoscopies and assist in patients' stratification, allowing accelerated patients management and individualized approach towards surveillance endoscopy.

Disclosure: Nothing to disclose

P1494

CHARACTERIZING CONSTIPATION SYMPTOMS AND MANAGEMENT STRATEGIES WITH DIGITAL DATA: A NOVEL APPROACH TO UNDERSTANDING REAL WORLD OUTCOMES

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Introduction: Understanding day-to-day variations in symptoms, behavior, and medication management can be important for improving patient centered outcomes for people with constipation. Patient Generated Health Data (PGHD) from digital devices is a potential solution, and the objective of this study was to assess the utility of PGHD as a marker of constipation symptom severity.

Aims & Methods: A virtual, 16-week prospective study of people with frequent constipation from an online platform connecting mobile digital devices including wearable monitors capable of collecting steps, sleep and heart rate data. Participants wore a Fitbit device for the study duration and were administered daily and monthly surveys assessing constipation symptom severity and medication usage. 38 predetermined day-level behavioral activity metrics were computed from minute-level data streams for steps, sleep and heart rate. Mixed effects regression models compared activity metrics between constipation status (irregular or constipated vs regular day) and medication use (medication day vs none, medication on irregular day vs medication or irregular day only, medication on constipation day vs medication or constipation day only) strategies as well as to model likelihood to treat with constipation medications based on daily self-reported symptom severity. Non-parametric ANOVA tests evaluated differences across treatment groups. Correction for multiple comparisons was performed with the Benjamini-Hochberg procedure for False Discovery Rate.

Results: 1,540 enrolled participants with completed daily surveys (mean age 36.6 sd 10.0, 72.8% female, 88.8% Caucasian). 1,293 completed all monthly surveys and 756 had sufficient Fitbit data density for activity analysis. 22 of the 38 activity metrics were significantly associated with bowel movement (BM) or medication treatment patterns for constipation. Compared to baseline regular days with no medication use, participants had fewer steps, longer periods of inactivity and reduced total sleep time on irregular and constipated days (Table 1). Participants were 4.3% (95% CI 3.2, 5.3) more likely to treat with medication on constipated days versus regular. Daily likelihood to treat increased for each 1-point change in symptom severity of bloating (2.4%, 95% CI [2.0, 2.7]), inability to pass (2.2%, 95% CI [1.4, 3.0]) and incomplete BM (1.3%, , 95% CI [0.9, 1.7]).

	Baseline	Change on irregular days	Change on constipated days	Change on medication days
Total steps [95% CI]	8887 [8627, 9147]	-200 [-280, -120]*	-96 [-200, 8]	-102 [-375, 171]
Maximum consecutive steps [95% CI]	1764 [1665, 1863]	-57 [-92, -22]*	-94 [-139, -48]*	95 [-24, 214]
Longest inactive period (minutes) [95% CI]	533 [525, 541]	9.1 [5.2, 12.9]*	0.1 [-5.0, 5.084]	9.9 [-3.2, 23.0]
Nightly sleep duration (minutes) [95% CI]	410 [404, 415]	-2.4 [-4.3, -0.4]*	-4.0 [-6.5, -1.4]*	-0.15 [-6.7, 6.4]
Sleep efficiency score (%) [95% CI]	91.12 [90.39, 91.85]	-0.10 [-0.19, -0.01]*	0.033 [-0.08, 0.15]	0.023 [-0.27, 0.31]

[Table 1. * Statistically significant to q-value < 0.05]

Conclusion: Constipation status irregular or constipated was associated with a number of activity metrics in steps and sleep. Given the small magnitude of effect, further research is needed to understand the clinical relevance of these results. Likelihood to treat with medication increased with increasing severity for a number of constipation symptoms. PGHD may be useful as a tool for evaluating real world patient centered outcomes for people with constipation.

Disclosure: SL, BBDF and RL are employees of Sanofi. BB, AS and WNL are employees of Evidation Health. Evidation Health performed the study which was sponsored by Sanofi.

P1495 WITHDRAWN

P1496

REPRODUCIBILITY OF HIGH-RESOLUTION OESOPHAGEAL MANOMETRY METRICS WITHIN A STUDY

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Introduction: Current guidelines suggest assessment of oesophageal motility with the use of high-resolution oesophageal manometry (HREM) by repeating measurements of motility after at least 10 water swallows [1]. However, reproducibility of the measurements may be questionable [2,3]. **Aim.** To compare reproducibility of repeated measurements of esophageal motility after 5 water swallows within a study

Methods: Patients referred for HREM (June 2019 -April 2020) to assess oesophageal motor function and/or to locate position of LES borders before pH-impedance study, and who gave consent to participate in the study were enrolled. The measurements were performed with a use of 36-channel 10 Fr solid state catheter (UniTip, Unisensor AG, the USA) and Solar Gastro software (MMS, the Netherlands) software by a standard technique in a sitting position [1]. At least 300 seconds after tube placement were allowed for adaptation.

During the study, patients made 10 water swallows by 5 ml each. An interval between the swallows was no less than 30 seconds. Two operators independently assessed the obtained results. After examinations were accomplished, the obtained measurements of 10 water swallows were divided into 2 series by 5 measurements each. These series were compared on the key oesophageal function metrics: the integrated relaxation pressure (IRP), the distal contractile integral (DCI), the distal latency (DL), together with contractile front velocity (CFV). Wilcoxon matched pairs test was used to compare these series of measurements (Statistica 10 (StatSoft Inc, USA)).

	Measurements 1 to 5 Mean±SD	Measurements 6 to 10 Mean±SD	P
Distal contractile integral, mm Hg x cm x sec	869.2±881.7	889.7±878.7	0.66
IRP 4, mm Hg	12.1±7.2	12.0±6.8	0.52
CFV, cm x sec	5.7±4.4	5.8±4.5	0.41

[Table 1. Values of series of measurements of the main studied metrics of esophageal motility]

Results: One hundred fourteen patients were enrolled. Among them are 46 men and 68 women, mean age (mean±SD) 48.8±11.5 years old. Of them, 52 patients with gastroesophageal reflux disease, 25 had different types of

achalasia and 37 had no oesophageal disorders. The inter-observer agreement reached 98%. No significant differences were found between the IRP, DCI, DL and CFV in 2 series of measurements.

Conclusion: No significant differences between two series of HREM measurements are found. according to the results, 5 water swallows may be enough to obtain sufficient details on standard evaluation of oesophageal motility. Reduction of time necessary for standard examination may allow additional time for functional tests (for example, for the assessment of solid food swallows, rapid drink challenge or multiple rapid swallows).

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Disclosure: Nothing to disclose

P1497

USING SIMULATION TO ENSURE BASIC COMPETENCE IN GASTROSCOPY

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Introduction: Esophagogastroduodenoscopy (EGD) is a commonly used procedure for diagnostic, treatment, or retrieval in the upper gastrointestinal tract. Operator competencies are essential for EGD quality, but no reliable test has been validated.

Aims & Methods: **Aim:** To develop and gather validity evidence for a simulation-based test and establish a pass/fail score in learning EGD.

Method: An expert panel in EGD and simulation evaluated the content of the Symbionix GI-mentor II simulator. Consensus reached on a test program including an intro-case, case 1 with a hiatal hernia and an esophageal diverticulum, and case 2 with a fundus tumor followed by the same EndoBubble case (popping 20 balloons in a pipe with an endoscope) repeated 3 times. A test was developed on an OGI CLA 4 phantom to test anatomical knowledge, technical skills with handling of forceps and retrieval of foreign bodies (a plastic bead and a suture).

Cases were divided into a diagnostic part including the two virtual reality cases and an examination of the phantom with identification of 15 landmarks in each case and 3 pathologies in total to test ability to identify anatomical landmarks and pathologies; as well as a technical skills part with evaluation of the EndoBubble cases and the retrieval tests.

A supervisor measured a multitude of parameters including: 1) total time for each test, 2) time to remove foreign bodies, 3) visualization electronically registered by the simulator, 4) wall hits and numbers of balloons popped in the EndoBubble cases.

We included 15 novices (medical students): N, 10 intermediates (endoscopy-assisting nurses): I, and 11 experienced (gastroenterologists >500 self-performed EGDs): E.

The contrasting groups' standard-setting method was used to establish a test with a pass/fail score.

Results: Mean total times for the diagnostic part were [minutes] N: 15.7±1.8, I: 11.3±1.0, and E: 7.0±1.5 and the technical skills part N: 7.9±2.5, I: 8.9±1.3, E: 2.9±0.6. The total numbers of the diagnostic landmarks and pathology identification were N: 26±5, I: 41±4, E: 48±0. Visualization percent was in case 1: N: 74±5, I: 69±4, E: 65±4 and case 2: N: 86±4, I: 73±7, E: 77±8. Mean numbers of wall hits was: N: 1.6±1.1, I: 9.4±3.8, E: 0.4±0.3 and mean numbers of total popped balloons was: N: 19.9±0.2, I: 19.2±0.3, E: 19.8±0.3.

A pass/fail standard score was established requiring the recognition of all landmarks and pathologies using a maximum time of 10.9 minutes in the diagnostic part and 4.6 minutes for the technical skills part. 10 experienced endoscopists passed all 3 requirements, while none of the novices or intermediates did.

Conclusion: We established a practical test that can distinguish between participants with different competencies. This enables an objective and evidence-based approach for assessing competencies for trainees undergoing an educational program in learning EGD.

Disclosure: Nothing to disclose

P1498

EFFECT OF EDUCATIONAL LECTURE ON DIAGNOSTIC ACCURACY OF JAPAN NBI EXPERT TEAM (JNET) CLASSIFICATION FOR COLORECTAL LESIONS

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Introduction: Japan NBI Expert Team (JNET) classification (the unified NBI magnifying findings classification for colorectal neoplasia in Japan) was proposed in 2016. However, the concrete education and training program of JNET classification has not been definitely established.

Aims & Methods: The aim of this study was to examine the diagnostic accuracy of JNET classification among beginners (students and initial residents) and less-experienced endoscopists before and after educational lecture on JNET classification. Seven beginners (4 medical students and 3 initial residents) without an experience of endoscopic diagnosis (the no endoscopy experience group, NEE group), 7 endoscopists with an experience of < 5 years in endoscopic diagnosis using magnifying NBI (the less-experienced endoscopists group, LEE group), and 3 endoscopy specialists with an experience of > 5 years in endoscopic diagnosis using magnifying NBI (the highly-experienced endoscopists group, HEE group) performed diagnosis using JNET classification for randomized NBI images of colorectal lesions (Type 1: 9 cases, Type 2A: 46 cases, Type 2B: 16 cases, Type 3: 9 cases) of 80 consecutive cases in our institution. Next, the NEE and LEE groups underwent an educational lecture (the HEE group did not take the lecture), after then all three groups made a diagnosis again for the 80 cases using JNET classification. We compared the diagnostic accuracy and interobserver agreement before and after the educational lecture. Further-

more, the sensitivity and specificity for each JNET type were investigated. The correct diagnosis for JNET classification was determined by diagnosis by the expert endoscopist (S.T.).

Results: In the LEE group, the correct diagnosis rate increased significantly after the lecture than before the lecture (66.6% vs. 86.4%, $P < 0.01$). Interobserver agreement improved after the lecture in the NEE and LEE groups (kappa value: 0.30→0.42 [NEE]; 0.38→0.74 [LEE]). In the NEE group, the high confidence rate of correct diagnosis was significantly increased after the lecture (18.8% vs. 36.6%, $P < 0.05$). In the NEE group, the sensitivity of JNET Type 1 (71.4%→88.9%, $P < 0.05$) and Type 3 (63.5%→73%, NS) tended to improve after the lecture.

However, even after the lecture, the sensitivity of JNET Type 2A did not improve well (55.9%→62.7%, $P < 0.05$) caused by mainly misdiagnosis as Type 2B. Moreover, the sensitivity of JNET Type 2B did not improve well (58.9%→64.3%, NS) after the lecture caused by mainly misdiagnosis as Type 3.

The specificity for each JNET Type in the NEE group tended to improve after the lecture (Type 1: 97.4%→97.6%, NS; Type 2A: 91.2%→94.1%, NS; Type 2B: 67.5%→72.5%, $P < 0.05$; Type 3: 90.5%→93%, $P < 0.05$). In the LEE group, for each JNET Type, the sensitivity (Type 1: 77.8%→96.8%, $P < 0.01$; Type 2A: 64.3%→86.3%, $P < 0.01$; Type 2B: 68.8%→86.6%, $P < 0.01$; Type 3: 63.5%→76.2%, NS), and the specificity (Type 1: 100%→99.4%, NS; Type 2A: 89.5%→97.9%, $P < 0.01$; Type 2B: 69.4%→87.3%, $P < 0.01$; Type 3: 95%→97.8%, $P < 0.05$) tended to improve after the lecture. In the HEE group, the sensitivity and specificity of all JNET types were good at around 90%.

Conclusion: Even with a less-experience in NBI magnifying observation, after an appropriate lecture on JNET classification, the diagnostic accuracy of JNET classification improved sufficiently, and even in beginners, the interobserver agreement and the accuracy rate of high confidence improved in a short time.

Disclosure: Nothing to disclose

P1499

COMPARISONS BETWEEN PATIENTS RECEIVING BOWEL PREPARATION EDUCATION TALK TWO WEEKS PRIOR COLONOSCOPY, INDIVIDUAL REMIND CALLS TWO WEEKS PRIOR COLONOSCOPY AND WITHOUT ANY REMINDER BEFORE THE COLONOSCOPY AND THEIR ADENOMA OR MORE ADVANCED LEISION DETECTION RATE

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Introduction: The average waiting time for colonoscopy in Hong Kong is 18 months. Patients are given the appointment slip, colonoscopy information sheets, bowel preparation instructions sheets and bowel preparation agents on the appointment booking date. Sometimes patients forget their appointments while some do not have their bowel preparation done properly. In our centre, some other out-patients clinics would refer their patients to our endoscopy centre for colonoscopy. These patients do not have any prior assessment in our hospital before the procedure. For our own hospital's patients, we offer them bowel preparation education talk two weeks prior colonoscopy. In the bowel preparation education talk, patients are educated the proper ways to take the low residue diet and the bowel cleansing agents.

A video is used during the talk to enhance patients' memories. If the patients do not attend the bowel preparation education talk, their colonoscopy appointment would be cancelled. During COVID-19 pandemic,

the bowel preparation education talk was temporarily suspended and replaced by individual remind calls 1-2 weeks prior colonoscopy. For patients referred from other clinics, they are educated on the day they get the colonoscopy appointment and do not receive any remind calls.

Aims & Methods: To compare the bowel cleanliness of the patients receiving bowel preparation education talk two weeks prior colonoscopy, individual remind calls two weeks prior colonoscopy and without any reminder before the colonoscopy. The polyp detection rate and adenoma or more advanced lesion detection rate among these groups of people would be compared.

Methods: 124 patients were recruited in this cross sectional study. 32 patients were in the bowel preparation education talk group, 34 patients were in the individual remind calls group, 58 patients were in the without any reminder group. Patients' bowel cleanliness were rated by endoscopists as good bowel preparation, fair bowel preparation and poor bowel preparation. The polyp detection rate and adenoma or more advanced lesion detection rate were reviewed.

Results: 13 patients receiving individual remind calls achieved good bowel preparation(38%), 4 patients in the bowel preparation education talk group achieved good bowel preparation(12.5%) and 3 patients in the without any reminder group achieved good bowel preparation(5%). The polyp detection rate for the bowel preparation education group was 17(53%), the individual remind calls group was 16(47%) and the without any reminder group was 22(38%). The adenoma or more advanced lesion detection rate for the bowel preparation education talk group was 11(34%), the individual remind calls group was 10(29%) and the without any reminder group was 14(24%).

Conclusion: Patients receiving individual remind calls achieved the best bowel cleanliness. The polyp detection rate and adenoma or more advanced lesion detection rate was highest in patients receiving bowel preparation education talk. Patients whom did not have any reminder prior colonoscopy were less likely to achieve good bowel preparation and hence lowered the polyp detection rate and adenoma or more advanced lesion detection rate.

Disclosure: Nothing to disclose

P1500

"BASIC" CLASSIFICATION FOR COLORECTAL POLYPS: EVALUATION OF THE EFFICACY OF A QUICK TRAINING

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Introduction: Advanced endoscopic imaging has revolutionized the characterization of polyps during colonoscopy. Many classifications (Kudo, NICE, Sano, WASP, CONNECT) were used based on the appearance of the pit pattern or vessels, the color or the macroscopic appearance of the polyps, the existence or not of a depression. A new BASIC classification including all of these criterias was proposed and validated for the BLI(FUJIFILM).

Aims & Methods: The main objective of this study is to evaluate the performance of non expert senior endoscopists after a rapid training(< 24 hours) in the characterization of colorectal polyps.

The study took place during endoscopy training days in June 2019. All participants had a theoretical training in different existing classifications. The next day, they had a presentation on the BASIC classification. An immediate evaluation included 20 quiz combining videos and photos for each case. All colic lesions had a diameter < 10mm. Of the 20 quizzes, 6 corresponded to hyperplastic polyps (PH), 10 to adenomas and 4 to sessile serrated adenomas. For each video, the participant had to indicate the final diagnosis and identify the 3 components used in the BASIC classification (aspect of the surface, existence or not of a pit pattern, the appearance of the vessels).

Results: 76 senior gastroenterologists participated in this study. The mean age was 34 years. 76% practiced in France and 24% in foreign countries. The mean number of colonoscopies performed per year was 100. The percentage of correct answers on the total number of quizzes was 55%. It was 50% for adenomas, hyperplastic and SSA/P respectively. There was no difference between doctors practicing in France and abroad. Less than 4% of gastroenterologists had a diagnostic score >90%.

Conclusion: Condensed training seems to be insufficient to acquire an acceptable level of reliability in the characterization of colorectal polyps. Will artificial intelligence replace the human intelligence in the upcoming years?

Disclosure: Nothing to disclose

P1501

MEASURING THE DISSEMINATION OF GASTROENTEROLOGY & HEPATOLOGY RESEARCH- AN ALTERNATIVE METRIC ANALYSIS OF MOST INFLUENTIAL RESEARCH ARTICLES

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Introduction: Bibliometrics such as citations analysis and Journal Impact Factor (JIF) have long been established as markers of scientific research quality and are used to measure the scholarly impact; however, they fail to measure the impact of research on the non-scientific population and the dissemination of knowledge from research to practice. These shortcomings have recently been filled by alternative metrics, which measure the attention articles receive in online media.

Aims & Methods: We aim to:

- determine the 100 most influential Gastroenterology and Hepatology (G&H) journal articles using alternative metrics;
- identify the factors influencing alternative metric scores; and
- analyze the relationship between alternative metrics and bibliometrics.

Altmetric.com search tool was used to determine the 100 most influential (G&H) journal articles based on their Altmetric Attention Scores (AAS). The online media factors that influence this score were then recorded. Bibliometric analysis of these articles was carried out to determine JIF, citations count, publication date, type of research, title of research, and country of origin.

Results: The AAS of the top 100 mentioned articles ranged from 2123 to 48. The most online media attention that contributed to the AAS came from USA and UK. The mean AAS, citations count, and JIF were 157.7, 63.68 and 16.49 respectively. Review journals such as *Nature Reviews Gastroenterology & Hepatology* (48) and *The Lancet Gastroenterology & Hepatology* (28) had the highest number of most mentioned articles, whereas the original research journals such as *Gastroenterology* (33), *Journal of Hepatology* (23) and *Hepatology* (19) had the most cited articles. The majority of the most mentioned and most cited articles originated from Europe and North

America with USA having the highest number of both, i.e. 35 and 57 respectively. Inflammatory bowel disease (15), gut microbiota (15) and functional GI disorders (10) were the most mentioned topics, whereas hepatocellular carcinoma (23), hepatitis C (20) and non-alcoholic fatty liver disease (22) were the most cited topics. Twitter mentions, Mendeley readers, news mentions, and Facebook mentions all showed positive association with Altmetric Attention Score. There was no significant correlation between Altmetric Attention Score and bibliometrics (citations count and JIF).

Conclusion: The dissemination of G&H research is multifarious across countries, journals and topics of research. Online media is an essential tool for researchers and publishers to rapidly disseminate newly created scientific knowledge and alternative metrics can be used to objectively measure this dissemination. Finally, alternate metrics in combination with bibliometrics provide an in-depth measure of the research impact.

Disclosure: Nothing to disclose

P1502

AN EVALUATION OF LEARNING IN NETWORKED COMMUNITIES TO IMPROVE KNOWLEDGE-BASED COMPETENCIES AND ENDOSCOPIC NON-TECHNICAL SKILLS WITHIN A NATIONAL CLINICAL ENDOSCOPIST TRAINING PROGRAMME

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Introduction: In the United Kingdom demand for endoscopy is increasing. National Programmes to provide structured training for Clinical Endoscopists (CE) have provided one means of increasing endoscopist capacity. Evaluation of initial cohorts of CEs identified the need for educational programmes to increase teaching content and methods to support the development of clinical reasoning and decision-making skills required for independent practice.

Aims & Methods: We aimed to assess learning needs related to knowledge-based competencies within current CE training programmes and evaluate different teaching strategies and social support mechanisms to assist group learning within the training programme.

Baseline learning needs were assessed during an introductory Academic Teaching Week (ATW) and by an online survey repeated after starting hands-on training. Correspondence via e-mail group and WhatsApp group recorded wider professional development issues and social contact within the group, allowing thematic analysis of subjects raised by group members, allowing assessment of social support on the learning process. Weekly Zoom tutorials, involving 2 tutors, were delivered using 5 different formats of case-based learning, linked to a pre-set curriculum and post-tutorial learning resources. A survey was sent to all participants to assess issues related to their learning, preferred learning environment and the extent to which different formats met learning needs.

Results: Feedback from 10 trainees engaged in current CE training programmes identified 6 main areas of clinical reasoning and decision-making as their main learning need - pre-endoscopy risk assessment; lesion recognition; differential diagnosis; classification; report-writing; investigation and management. Feedback from the ATW demonstrated learning in these areas. Five formats for Zoom tutorials were compared based on survey responses and post-session transcript analysis for parameters of active learning and discussion.

Survey responses indicated a preference for case-based learning or assessment linked to specific feedback. This was more valued than open discussion. The Zoom platform especially the facility to share screen content was highly acceptable to all trainees and technical issues were rare.

For CE learners, social support networks are most active in response to specific professional challenge e.g. contracts, hands-on training events. Peer group learning and the ability to interact was highly valued.

Conclusion: Zoom tutorials blended with social media tools and aligned to a learning curriculum can effectively meet knowledge-based learning needs. Case-based lesson plans or assessment with feedback provided the optimum learning environment for trainees. Scheduled Zoom sessions can be scaled up to include larger numbers of trainees and provide an opportunity to assess longitudinal trainee development.

Disclosure: NH acts as a Company Director for Gastro-e-Learn PD nothing to declare

P1503

EVALUATION OF THE INITIAL PHASE OF A CLINICAL ENDOSCOPIST COLONOSCOPY TRAINING PROGRAMME PILOT IN WALES

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Introduction: Demand on endoscopy services requires an increased clinical endoscopist workforce in Wales. To ensure safe and effective practice a comprehensive longitudinal training programme has been developed. This comprises two academic training weeks; a University based Level 7 Academic module; simulator training; Joint Advisory Group in GI Endoscopy (JAG) Hands-on basic training course; training lists with a clinical supervisor (2 per week); online SLATE lesion recognition training courses; endoscopic non-technical skills (ENTS) training and JAG Polypectomy course. We report on the evaluation of the early phase of a National Clinical Endoscopist Training programme pilot.

Aims & Methods: 1) To assess feasibility of implementation of a National Training Programme.

2) To evaluate initial outcomes from the programme.

Structured feedback on each element of training programme delivery was received from delegates and faculty. Trainee completion of academic components of the course is assessed by University tutors. The clinical progress of trainees can be tracked using the JETS e-portfolio used by all UK endoscopy trainees. Case progression rates of the CE trainees were compared against 'controls' on Gastroenterology Speciality Trainees (Wales Deanery) at the same stage of endoscopy training.

Results: All clinical endoscopists with the programme rated as excellent or very good the knowledge-based content delivery in the Academic Training weeks. Sessions on professional development were particularly valued and having a nurse endoscopist as part of the training faculty was identified as important. Academic progress of all trainees through the level 7 modular components has been satisfactory.

Simulation training was affected by the breakdown of a computer simulator, but this was substituted with alternative models. Trainees rated simulation as useful in refining scope handling technique. Evaluation of online SLATE courses was positive and additional face-to-face training on lesion recognition was also highly valued. Clinical progression of hands on cases has been satisfactory, with average quarterly case progression comparing favourably to speciality trainee controls (38 vs 30 cases/qtr) and all trainees remain were course to achieve certification for independent practice in colonoscopy within 2 years. The COVID-19 epidemic has delayed ENTS and polypectomy training and analysis will account for temporary suspension of the programme.

Conclusion: It is feasible to deliver this type of longitudinal training programme for clinical endoscopists. Further investment in endoscopic simulators has resulted from assessment of this aspect of training, all

other elements were rated highly in training and faculty feedback. Health Education and Improvement Wales have commissioned a further cohort of clinical endoscopists to commence a National Clinical Endoscopist Programme in upper and lower GI endoscopy based on this model.

Disclosure: NH acts as a company director for Gastro-e-Learn PD nothing to declare

P1504

BURNOUT IN GASTROENTEROLOGISTS: A NATIONAL-LEVEL ANALYSIS

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Introduction: The term burn-out or burnout, means “burn to exhaustion”. According to Freudenberg, burnout is a “state of physical and mental exhaustion conditioned by the individual’s professional activity”. Burnout manifests itself through a set of signs and symptoms associated with physical and emotional breakdown that result from total energy exhaustion, lack of resources or forces available to “help” others.

Aims & Methods: This study aims to assess the prevalence of burnout in Portuguese gastroenterologists and understand how certain sociodemographic and professional variables might be associated with burnout appearance.

This is an observational descriptive, prospective and multicenter study. It was analyzed data related to a sample of 52 gastroenterologists at national level, in the period between February 5, 2019 and April 13, 2019. An estimate of the burnout levels was carried out by the Copenhagen Burnout Inventory (CBI) questionnaire validated for the Portuguese population - CBI-PT. Possible interconnection between sociodemographic and socio-professional variables were analyzed.

Results: More than half of the gastroenterologists surveyed did not experience burnout in all subscales of the CBI. In the personal level, 13 gastroenterologists with moderate burnout and 11 with high burnout were registered. Regarding the work extent, 18 gastroenterologists with moderate burnout and 7 with high burnout were registered. In relation to the patient extent, 21 gastroenterologists with moderate burnout and 3 with high burnout were registered. There were no cases of severe burnout. Physicians who developed burnout were significantly younger ($p < 0.001$), have shorter service time ($p = 0.007$) and devote less time to leisure ($p = 0.024$). Doctors in the internship have a higher prevalence of burnout, which might be significantly related to a higher level of professional stress ($p = 0.016$). Likewise, performing certain exams (varicose ligation and endoscopic capsule) or performing high amount of techniques (upper gastrointestinal endoscopy and colonoscopy), as well as doctors working at the weekend or being accused in medico-legal issues had been shown to be associated with a higher prevalence of burnout.

Conclusion: A higher prevalence of burnout was identified in young gastroenterologists, doctors in the internship, those performing high amount of techniques (upper gastrointestinal endoscopy and colonoscopy), as well as doctors working at the weekend or being accused in medico-legal issues. If these young doctors do not acquire tools that allow them to deal with this problem, it is expected that this pathology will reach critical values in gastroenterologists, with a consequent negative impact on health-care.

Disclosure: Nothing to disclose

P1505

IMPLEMENTATION OF INTERPROFESSIONAL COLLABORATION INTO THE EDUCATION OF YOUNG HEALTH CARE PROFESSIONALS VIA ESTABLISHMENT OF INTERPROFESSIONAL TRAINING WARDS (“A-STAR”, “IM A-STAR”)

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Introduction: Over the last decade interprofessional collaboration has been steadily gaining importance in everyday working routines in hospitals and out-patient clinics all around the world. To achieve the implementation of interprofessional working standards and fully incorporate them into the staffs work ethic, there needs to be a change in the way young doctors and nursing staff are trained. We established an interprofessional training ward for last year medical students and second to third year nursing students, for the treatment of unselected patients with diseases from the whole spectrum of gastroenterology. Supervision and training are overseen by residents and nurses’ practitioners with additional designation in teaching.

We further included pharmacology students and students of the newly created branch of molecular medicine, whenever possible into teaching rounds to open up a broader spectrum of interprofessional collaboration.

These students profited from getting close insights into clinical practice at bedside and were therefore able to connect their knowledge and research to real-life cases. In turn, clinicians and nursing students gained first-hand knowledge of the process of drug development, testing and research, thus strengthening the bridge between research and clinical practice.

To enable close communication, we not only established a common workspace, but also implemented shared morning briefings, teaching rounds and regular rounds on the ward and shared interprofessional briefings into everyday working routine.

Aims & Methods: In order to monitor and evaluate the students experience in the training wards, we created a whole set of questionnaires, aimed at keeping track of the students professional and personal progress, as well as perceived interprofessional collaboration, using standardized questionnaires and scoring systems.

The purpose of the ongoing evaluation is to assess the effectiveness of an interprofessional practice curriculum in improving interprofessional collaboration and communication as well as knowledge and clinical skills. Based on a pre-post questionnaire design, effects were measured by:

- 1) the German version of the ‘Collaboration and Satisfaction About Care Decisions (CSACD)’ developed by Baggs (1994) (permission for translation and validation was obtained; pre-test design),
- 2) the German version of The UWE (University of Western England) Entry-Level Interprofessional Questionnaire developed by Pollard (2004).
- 3) Additionally, satisfaction with the programme, content, clinical skills, learning process and teaching methods was analysed with a course evaluation form (University Hospital Regensburg; post-test design).

Results: In our interim analysis we experienced a thoroughly positive feedback from medical and nursing students alike. Not only did they benefit of each other in their learning on a professional level, but most of them reported a notable improvement in their communication skills and on a personal level, including abilities in leadership, conflict management and self-esteem/empowerment.

Conclusion: These positive results led to the expansion of the interprofessional training ward “A-STAR”. We included our intensive care unit into the program (IM A-STAR), providing medical students with the possibility to expand their training to critically ill patients and train their skills in inter-professional with the ICU nursing staff.

To our knowledge this is a unique concept so far, and can lead to be a model for other hospitals seeking to improve their interprofessional collaboration in early stages of medical and nursing students education.

Disclosure: Nothing to disclose

P1506

THE EFFECTS OF SEX AND AGE DIFFERENCES ON GASTRIC CANCER IN TERMS OF INCIDENCE OF HISTOLOGIC SUBTYPES AND SURVIVAL RATE IN KOREA

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Introduction: Gastric cancer (GC) incidence rate in male is about two times higher than that of female in both high and low-risk areas. Diffuse-type gastric cancer occurs more in female, younger patients compared to intestinal-type gastric cancer. These differences might be explained some parts by effects from sex hormones. However, few reports have been reported regarding sex and age differences of Lauren histologic subtypes of GC.

Aims & Methods: The aim of this study is to evaluate the effects of sex and age differences on GC through incidences of Lauren subtype and survival rate of GC.

From May 2003 to December 2019, we enrolled 3314 patients with GC prospectively and they were treated with endoscopic or surgical treatment at Seoul National University Bundang Hospital. After dividing all patient into three different age (<40, 40-64 and 65 years ≤), clinicopathologic characteristics including Lauren histologic classification and survival rate was analyzed.

Results: Among 3414 patients with GC, 2252 (67.9%) were male and 1062 (32.1%) were female. In female patients, the proportion of diffuse-type GC showed dominance compared to male (50.7% vs 27%; $p < 0.001$) (Table), highest in subgroup age under 40 and a downward trend with age in female (<40, 40-64 and 65 years ≤: 91.5%, 60.9% and 30.6%; $p < 0.001$). In contrast the proportion of diffuse-type in male was quickly decreased as getting old (<40, 40-64 and 65 years ≤: 77.9%, 33% and 16.7%; $p < 0.001$). There were significantly higher current *H. pylori* positivity in female than that of male (59.7% vs 53.8%; $p = 0.002$), especially in the age of 40-64 years old (66.5 vs. 60.2; $p = 0.014$). Similar higher trend of lymph node metastasis was found in female than that of male (27.8% vs 23.6%; $p = 0.010$), especially in the age 65 ≤ (28.7% vs 21.4%; $p = 0.003$). However, the remaining TNM staging was not different between male and female.

The overall survival (OS) of female patient was significantly higher than male patient in total group and in subgroup age 65 ≤ (75.9% vs 65.6%; $p = 0.002$, 62.5% vs 45.6% $p = 0.015$). In subgroup age under 40, female had poor OS compared to male, but there was no statistical significance (84.5% vs 86.8%; $p = 0.779$).

The cumulative GC specific survival (GC-SS) of female patients was lower than male patients in all subgroups, but there was no statistical significance by Kaplan-Meier method. Unfavorable prognostic factors associated with poor GC-SS were older age, diffuse type histology, degree of gastric wall invasion, lymph node metastasis and metastasis to another organs.

Conclusion: In gastric cancer patients, female shows higher incidence of diffuse-type GC than male but there was no difference of GC-specific survival rate regardless of age between male and female.

	Male			<i>p</i> -value	Female			<i>p</i> -value
	Total (%)	Intestinal	Diffuse		Total (%)	Intestinal	Diffuse	
<40 (%)	68 (3.0)	15 (22.1)	53 (77.9)	<0.001	94 (8.9)	8 (8.5)	86 (91.5)	<0.001
40-64 (%)	1176 (52.2)	788 (67.0)	388 (33.0)		514 (48.4)	201 (39.1)	313 (60.9)	
65 ≤ (%)	1008 (44.8)	840 (83.3)	168 (16.7)		454 (42.7)	315 (69.4)	139 (30.6)	
Total (%)	2252 (100)	1643 (73)	609 (27)		1062 (100)	524 (49.3)	538 (50.7)	

[Proportions of intestinal and diffuse subtype gastric cancer in male and female subgroups according to different age group.]

Data are presented as number (%).

p-value was calculated using; Chi-square test for categorical variables.

Bold style indicates statistical significance.

Disclosure: Nothing to disclose

P1507

CLINICAL CORRELATES OF LEFT-HANDEDNESS ADULT PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: The prevalence of left-handedness (LH) in functional gastrointestinal disorders (FGID) remains discussed. We aimed to search the frequency of LH in FGID defined according to Rome criteria.

Aims & Methods: 2178 outpatients filled out the Rome III questionnaire for FGID, Beck Depression Inventory, State and Trait Anxiety Inventory, Bristol stool form, and four ten-point Likert scales for the report of the severity of constipation, diarrhea, bloating, and abdominal pain. They also answered a question about laterality, Left-handedness, or Right-handedness. A logistic regression model adjusted for gender, age, BMI, FGID, depression, anxiety with the right-handedness as the reference group was created.

Results: LH was reported by 114 patients (5.2%). They reported a similar prevalence of esophageal, gastroduodenal, and anorectal disorders. The multivariable logistic regression analysis shows that LH patients have lower body mass index ($P = 0.006$; OR=0.951; 95%CI=[0.918-0.986]), higher state anxiety ($P < 0.001$; OR=1.034; 95%CI=[1.019-1.050]), and reported lower prevalence of irritable bowel syndrome (IBS) ($P = 0.004$; OR=0.519; 95%CI=[0.330-0.815]) and the subtypes IBS-Constipation ($P = 0.003$; OR=0.243; 95%CI=[0.096-0.614]), and IBS-Mixed ($P = 0.031$; OR=0.273; 95%CI=[0.084-0.887]) and a higher prevalence of IBS-Unspecified ($P = 0.027$; OR=1.971; 95%CI=[1.082-3.591]), and abdominal pain ($P = 0.020$; OR=2.025; 95%CI=[1.117-3.671]).

Conclusion: In FGID patients, LH is associated with painful bowel disorders without motility disorders, suggesting a relationship of cerebral lateralization with FGIDs.

Disclosure: Nothing to disclose